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COMPILATION OF ARTICLE SUMMARIES FROM ETS/IAQ REPORT

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— TABLE OF CONTENTS —

LUNG CANCER 1

CARDIOVASCULAR ISSUES 9

RESPIRATORY DISEASES AND CONDITIONS - ADULTS 11

RESPIRATORY DISEASES AND CONDITIONS - CHILDREN 15

OTHER CANCER 21

OTHER HEALTH ISSUES 23

ETS EXPOSURE AND MONITORING 30

INDOOR AIR QUALITY 45

SMOKING POLICIES AND RELATED ISSUES 48

STATISTICS AND RISK ASSESSMENT 50

INDEX 53

Please note: This document is not intended to be an encyclopedic summary of scientific literature relating to ETS. Rather, it only contains summaries and excerpts from those studies included in *Reports on Recent ETS and IAQ Developments.*

The summaries contained in this document are intended as a reference; the actual articles should be consulted for any purpose beyond a summary reference.

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ENVIRONMENTAL TOBACCO SMOKE & INDOOR AIR QUALITY

ARTICLE SUMMARIES FROM ETS/IAQ REPORT

LUNG CANCER

[1] Cummins, D., "Pets and Passive Smoking," *British Medical Journal* 309: 960, 1994 [Issue 85, Item 25]

In this letter to the editor, the author comments that one of his patients, who had smoked more than 40 cigarettes daily, had owned two dogs that had died of lung cancer and a cat that "had suffered from chronic wheezing that resolved when the patient discontinued smoking." The author suggested that this observation, and similar claims published elsewhere, might be a "powerful weapon with which to assail smokers."

[2] Lee, P.N., "An Assessment of the Epidemiological Evidence Relating Lung Cancer Risk in Never Smokers to Environmental Tobacco Smoke Exposure." In: *Environmental Tobacco Smoke.* H. Kasuga (ed.). Springer-Verlag, 28-84, 1993 [Issue 82, Item 30]

This extensive literature review condenses and updates Lee's 1992 book on the epidemiology of ETS. Lee also criticizes the EPA Risk Assessment on ETS for a number of methodological shortcomings.

EXCERPTS:

"The purpose of this paper is to review the overall evidence [on ETS and lung cancer]. . . . Several major reviews of the subject have been published . . . All these reports have concluded that ETS exposure causes lung cancer. Based on a more detailed evaluation, my review questions this conclusion and highlights the limitations of these earlier reviews. This review is a shortened and updated version of a larger review published in book form in 1992, the reader being referred to the latter for additional detail."

"This review focuses on 33 epidemiological studies of lung cancer for which results have been separately presented for lifelong never smokers. . . . The list includes all those included in the EPA meta-analyses with the addition of recently published studies by Brownson and Stockwell, and a further study by Kabat for which results have only been presented at a conference."

"Although there are no currently available methods of objective quantification of lifetime ETS exposure, it is important to note that none of the studies have attempted to quantify current ETS exposure objectively."

"Using adjusted results where available . . . seven of the 33 studies reported a statistically significant increased incidence of lung cancer among nonsmoking women married to or living with a smoker when compared with nonsmoking women married to or living with a smoker when compared with nonsmoking women married to or living with a nonsmoker, and one reported a statistically significant decreased incidence. Only one of the 10 studies on males reported a statistically significant increase and none a statistically significant decrease."

"For females there is a statistically significant association (95% C.I. 1.08-1.35) between risk of lung cancer in never smoking women and the index 'marriage to or living with a smoker.'"

"When all the results are considered, there is no statistically significant evidence of an association between workplace ETS exposure and risk of lung cancer in never smokers. Of the 15 estimates . . . nine are greater than 1.0 (two marginally significantly so), one equal to 1.0, and five less than 1.0, and all the meta-analysis estimates . . . are close to 1.0. A further two studies, not included in the meta-analysis, reported finding no association, but gave no detailed data. . . . There was also no evidence of a relationship between childhood ETS exposure and risk of lung cancer in never smokers. Of the 16 estimates . . . seven are greater than 1.0, one equal to 1.0, and eight less than 1.0, and all the meta-analysis estimates . . . are slightly, but not significantly, less than 1.0. A further two studies, not included in the meta-analysis, reported finding no association but gave no detailed data."

"The overall results indicate that risk of lung cancer in never smokers is not associated with exposure to ETS in childhood or in the workplace. In contrast they indicate a weak association with marriage to or living with a smoker, with risk increased by about 20%. There are in theory two alternative reasons for this apparent conflict of results between the findings for marriage to or living with a smoker and those for childhood and workplace exposure. First, it is possible that the association with marriage to or living with a smoker results from bias. . . . Second, it is possible that marriage to a smoker is a much better

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marker of ETS exposure than is working with a smoker or having a parent who smoked in childhood."

"Some studies report finding significant dose-related trends, but these analyses typically include the nonexposed group so that they duplicate to a considerable extent the simple comparison of exposed and unexposed individuals. . . . Such analyses do not answer the question as to whether risk increases with exposure in the exposed groups."

"[O]ne would not expect, if ETS really affected risk of lung cancer, to find some studies claiming an association with one histological type and other studies claiming association with another histological type. In fact the evidence . . . is rather inconsistent."

"This lack of a clear relationship with a specific type of lung cancer weakens the argument for an effect of ETS exposure."

"For the 11 studies published from 1989 onwards, which include the large Wu-Williams and Brownson II studies that reported estimates at or less than 1.0, the relative risk estimate is close to 1.0. . . . It might perhaps reflect a tendency towards larger and more carefully conducted studies. It might also reflect the fact that the earliest studies published on any issue tend to be statistically significant."

"[T]here is by now strong evidence from a number of other studies that marriage to a smoker or living with a smoker is associated with increased exposure to other lung cancer risk factors."

"This evidence has now been supplemented by detailed analysis of extensive data from the British Health and Lifestyle Survey . . . In this study we identified 33 lifestyle 'risk factors,' i.e., factors generally perceived to be associated with adverse health consequences, not necessarily with increased lung cancer risk. Of the 33 risk factors, 27 showed a highly significantly increased prevalence in smokers of 20+ cigarettes per day compared to never smokers, and only two showed a decreased prevalence."

"Though some of these differences are for factors not related to lung cancer risk, many are, including high fried food and low fruit and vegetable consumption, occupation, low social class, poor education and high alcohol consumption. It is clear also from these results that the magnitude of potential bias due to these risk factors is important in comparison to the magnitude of the associations . . . especially when one considers that bias due to confounding by multiple risk factors will be greater than that due to individual risk factors."

"[T]hough this area needs clearer data, it seems that working with a smoker should be a marker of increased ETS exposure, perhaps as good as marriage to a smoker in terms of current exposure."

"As the discussion above has shown, the epidemiological evidence on ETS and lung cancer risk in never smokers is much weaker than the EPA report (and also other published reports) makes it appear."

"Furthermore, there are a number of glaring omissions in the EPA report, with evidence that is inconsistent with the EPA's hypothesis not being presented despite being pointed out by myself and others in written and oral submissions to the EPA."

"Failure to consider workplace and childhood ETS exposure. . . . Unless there are strong reasons to believe that smoking by the spouse is a much better marker of ETS exposure than is smoking in the workplace or smoking by the parent in childhood, and the EPA does not discuss such reasons, it clearly biases the whole presentation to fail to report results for these two alternative indices that show no association at all with lung cancer risk and to concentrate solely on the single index that arguably does show an association, albeit an extremely weak one."

"Failure to take into account properly the possibility of confounding. . . . There are three fundamental flaws in the EPA's argument. First, they appear to require one risk factor to explain the whole of the observed association. This is clearly far too stringent a requirement. Bias might arise from many sources, of which confounding is only one. More than one risk factor might confound. Second, when trying to determine whether a factor actually elevates lung cancer risk, attention was largely restricted to evidence collected in the ETS/lung cancer studies themselves, even though there is abundant relevant data from other sources. Third, they ignore the growing evidence that ETS exposure is associated with increased exposure to diet and other risk factors and fail to reach the appropriate conclusion that a nonsmoker married to (or living with) a smoker is generally more exposed to other risk factors than is a nonsmoker with no smoker in the household. The question is not whether confounding exists. The question is what magnitude it has."

"Failure to correct fully for bias due to misclassification of active smoking. . . . [T]he EPA could well have markedly underestimated the extent of bias from this source."

"Failure to consider histological type. . . . A major weakness of the EPA report is that it makes no attempt to compare and contrast results for these two major

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types of lung cancer. Consistency is a criterion that is cited for testing causality but is not actually applied in this context."

"Failure to address publication bias. . . . There is, in fact, some evidence that relative risks are greater in small studies, indicating failure to publish small studies reporting no association. . . . It is actually not impossible that results from some large studies have not been published."

"Failure to test for effects of study weaknesses. . . . Surprisingly, however, [EPA] did not attempt to compare relative risk estimates of studies according to specific weaknesses."

"Over interpretation of the dose-response data. . . . Where there is evidence in a study of an increased risk in the exposed group, a trend analysis provides additional evidence if it is conducted on the exposed groups only. The EPA has not conducted such analyses but has always included the nonexposed group in their analysis. Though there is some evidence of a dose-response relationship when only exposed subjects are considered, it is much weaker than indicated by the EPA."

"When one takes all the above considerations into account, it is clear that the epidemiological evidence does not convincingly support the notion that ETS exposure causes lung cancer. The possibility that ETS exposure does lead to a small risk of lung cancer must remain since it is not logically possible to prove a negative. However, it is clear that estimates of thousands of lung cancer deaths occurring annually in U.S. nonsmokers as a result of ETS exposure are meaningless."

"To say, as the EPA does, that the overall confidence in their estimate of 3,000 lung cancer deaths per year due to ETS is 'medium to high' is absolutely unjustifiable. The number could as well be 300, 30, 3 or even 0.3. The truth is that it has not even been demonstrated that any lung cancer deaths result from ETS exposure."

[3] **Letters to the Editor Regarding Rennie, D., "Smoke and Letters," *Journal of the American Medical Association* 270(14): 1742-1743, 1993 [Issue 86, Item 28]**

Correspondence continues to be published in the *Journal of the American Medical Association* concerning Drummond Rennie's editorial (*See* issue 58 of this Report, October 22, 1993), on the 1992 Trichopoulos, et al., study on lung tissue changes in nonsmokers reportedly exposed to ETS (*See* issue 32 of this Report, October 9, 1992). The most recent exchange, between Peter N. Lee and the editors of *Tobacco Control*, Ronald M. Davis and Simon Chapman, appears at *Journal of the American Medical Association* 272(19): 1479-1480, 1994.

In his letter, Mr. Lee suggests that Davis and Chapman were "attempting indirectly to smear [his] work...without giving any indication whatsoever as to the basis of their criticisms" in a previous letter to the editor. He also takes issue with Davis' and Chapman's "suggestion that [he] would deliberately mislead," calling it "without basis...insulting and potentially damaging" to his relationship with his clients. Mr. Lee also noted that part of a sentence was inadvertently omitted in his original letter criticizing the Trichopoulos, et al., study.

Mr. Lee proposes that Trichopoulos, et al., "wrote a poor article and were justifiably criticized for it." He also states that Davis and Chapman, in their earlier letter, "were wrong to imply that the criticisms were unfounded, and even more so to attempt to attack tobacco industry consultants and employees without giving a shred of supportive evidence." He concludes by stating that "it seems inadvisable for editors to publish unsupported criticisms, irrespective of whether the correspondents are funded by the tobacco industry or by antismoking organizations."

In their reply, Davis and Chapman claim that their original letter did not cite Lee's letter, and thus disagree with Lee's position that they were attempting to "smear" his work. To support their criticisms of industry-funded letters, they characterize a 1993 letter by Dr. Sharon Boyse on the EPA Risk Assessment on ETS as "misleading." They also claim that "[i]nternal industry documents that have surfaced recently suggest that the industry's research enterprise is nothing but a public relations sham." They conclude by calling for "special scrutiny" for tobacco industry consultants, stating "vested interests and financial arrangements cast a serious shadow of doubt over any scientific pronouncements that emanate from the industry and its commissioned researchers."

Previously published letters are discussed in the following past issues of this Report: issue 58, October 22, 1993; issue 67, March 4, 1994; and issue 76, July 15, 1994.

[4] **Thornton, A., Lee, P., and Fry, J., "Differences Between Smokers, Ex-Smokers, Passive Smokers and Non-Smokers," *Journal of Clinical Epidemiology* 47(10): 1143-1162, 1994 [Issue 86, Item 27]**

Based on a sample of more than 9,000 British adults, the authors of this study report that certain lifestyle variables, which may be associated with disease risk, vary among smokers, nonsmokers, and persons reporting exposure to ETS. They caution that such risk factors

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could be confounders in epidemiologic studies of "passive smoking."

EXCERPTS:

"Because smokers and passive smokers are not a random selection of the population, such studies have always to take into account the theoretical possibility that observed differences between the groups studied may arise, at least in part, due to differences in exposure form other risk factors and not wholly to effects of smoking or of environmental tobacco smoke exposure."

"Differences between non-smokers exposed and not exposed to environmental tobacco smoke are less well studied, though recent reports have pointed to a possible confounding of the lung cancer relationship by diet."

"Firstly, smokers tend to have unhealthier lifestyles than non-smokers in a number or respects, so that they would be expected to have higher rates of many diseases even in the absence of any effect of smoking. Secondly, for many of these lifestyle factors passive smokers are also somewhat worse off than non-smokers are also somewhat worse off than non-smokers in a number of respects, so that they would be expected to have higher rates of many diseases even in the absence of any effect of smoking. Secondly, for many of these lifestyle factors passive smokers are also somewhat worse off than non-smokers unexposed to environmental tobacco smoke. Thirdly, bias due to confounding may well be important for diseases weakly associated with active smoking and for diseases associated with passive smoking (where associations reported are usually weak)."

"The objective of the work described here was to confirm these provisional conclusions on a large representative database with extensive information on a variety of lifestyle factors. . . . Because of the range of deceases that have been associated with smoking and passive smoking, and the range of lifestyle factors that have been linked to these diseases, we do not make any formal attempt here to determine which associates are, and which associates are not, importantly affected by confounding."

"Two associates with passive smoking are clearly directly related to its definition. thus divorced, separated or widowed people are clearly much more likely to live on their own so being in the base group, while respondents living in larger households are clearly more likely to contain smokers. With these exceptions, it was evident that there were many risk factors for which passive smokers showed increases in the same direction as current smokers, though the increase was generally of a smaller magnitude. Thus, like current smokers, passive smokers tended to be less educated; of lower social class; work in 'risky' occupations; drink more alcohol; do nothing to keep healthy; take longer before their first meal of the day; eat more fried foods and bread; eat less cereal, fruits, salads and low fat/polyunsaturated spread; drink more tea (but not more coffee; use more sugar in tea and coffee; not cut down on fatty foods; and be more neurotic and extrovert. They were also less likely to eat sweet foods. Of these risk factors, only for fried foods and bread, where consumption by passive smokers was similar to that of current smokers, was the prevalence of passive smokers not intermediate between that of current smokers and the base group. Prevalence of many risk factors was higher in passive smokers than in ex-smokers. Adjustment for household size (1, 2, 3+), in addition to sex and age, did not affect the general conclusions."

"Respondents were also asked whether either of their parent had ever smoked, though information was not collected as to whether they had smoked when the respondent was a child. . . . Compared with those where neither parent smoked, never smokers, having two parents who smoked, drank more alcohol; ate more bread and were more extroverted; ate more fried food, drank more coffee and more often had a type A personality; and were more neurotic. They also showed significant decreases for some risk factors. Thus never smokers with two smoking parents were less likely to have ever tried to lose weight; were more likely to use low fat/polyunsaturated spread and to be cutting down on fatty foods; and ate less sweet foods and were less often underweight. The associations with alcohol consumption, bread and fried foods were also evident in those where the father only smoked, while where the mother only smoked only the association with alcohol consumption was evident, though very clearly. Generally risk factors associated with current smoking correlated much better with risk factors associated with passive smoking as indexed by living with a smoker than with risk factors associated with passive smoking as indexed by having parents who smoked."

"The extent to which the relationship of a disease to current, ex-, or passive smoking will be biased by confounding by a single risk factor depends not only on the prevalence of the factor in the groups being compared but also on the relative risk of disease by level of exposure to the factor."

"For many of the risk factors considered, the relationship of prevalence to current, ex- and passive smoking formed a consistent (or nearly consistent) pattern, with the following typical characteristics;

(i) increase in current cigarette smokers (compared to never smokers) which is dose-related, the highest

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prevalence being seen in smokers of 20+ cigarettes per day;

(ii) decrease in prevalence with increasing time given up smoking, with long term (20+ years) ex-smokers having similar prevalence to never smokers and short term (1-9 years) ex=smokers having a higher prevalence than never smokers, but a lower prevalence than current smokers;

(iii) increased prevalence in never smokers living with smoker than in smokers living alone or with no smokers, the increase being less than that seen in relation to current smoking."

"For many risk factors this pattern was clearly evident in both sexes. . . . The observed differences in prevalence of risk factors in relation to passive and ex-smoking could not be explained by misclassification of current smoking status, since omitting from analysis the relatively small proportion (2.3%) of never and ex-smokers who had high carbon monoxide levels, on the basis that they were likely actually to be current smokers, did not materially affect our conclusions."

"For most risk factors the differences in prevalence observed between current, ex, passive and non-passive smokers were really quite similar for younger (<50) and older (50+) subjects. . . . [T]he tendency for smokers to have less education and to drink more is much more strongly seen in the younger group, while the association of smoking with unemployment, hours slept and frequent coffee drinking is hardly, if at all, evident in the older group. For these exceptions, therefore, it is important, when using our findings as an aid to interpreting results of studies relating smoking or passive smoking to health, not to over-generalize."

"The tendency for smokers to have a more risky lifestyle than non-smokers is, however, abundantly clear form our data and is a conclusion that does not depend at all on precisely which risk factors we chose to present detailed results for out of the many for which we had data."

"Our study showed clearly that current smokers consumed more fried foods and bread and less breakfast cereal, fruits and salads than never smokers and similar differences were also seen comparing passive smokers with never smokers. Presumably the association with passive smoking arose because non-smokers married to smokers tended to share, at least in part, the diet of a smoker."

"Consumption of sweet foods was a 'typical' risk factor but int he reverse direction, being the only clear example of a factor generally thought to be harmful which smokers were less exposed to."

"Although we have demonstrated that many risk factors are associated with various aspects of the smoking habit and that confounding may arise as a result, it is not straightforward to estimate precisely the extent of bias due to confounding in any particular situation."

"It is evident from the material presented here that bias due to confounding is likely to be of much more practical importance for diseases that are weakly associated with smoking than for diseases that are strongly associated."

"Weak associations, particularly those with relative risks less than 2 and especially those with relative risks less than 1.5, are, however, much more likely to arise as an artifact arising form confounding. This is of particular importance when considering associations with environmental tobacco smoke exposure. . . . [A]n increased risk of lung cancer in never smokers married to or living with smokers, . . . is now, based on the latest data estimated at only 1.17. Although, as judged by the 95% confidence limits (1.08-1.27), the association is statistically significant, there is a distinct question mark as to whether it arises as a result of a causal relationship or as a result of bias. . . . 'Marriage to a smoker', as an index of ETS exposure, is subject to bias from two sources. One bias results from the fact that some current or past smokers tend to deny they have ever smoked, the tendency of smokers to marry smokers leading to a greater proportion of misclassified smokers or ex-smokers in the group classified as 'never smokers married to a smoker' than in the group classified as 'never smokers married to a non-smoker'. The second bias results from the fact that the group married to a smoker are more exposed to other risk factors than are the comparison group. the analyses described here support the view that this second source of bias is important. thus the analyses demonstrate that passive smokers have an increased prevalence of exposure to (at least) five lifestyle factors (low social class and working in 'risky' occupations; increased alcohol drinking; increased consumption of fried foods; reduced consumption of fruits and salads; increased neuroticism), all of which have been reported as having been associated with an increased risk of lung cancer."

"Generally, the results of this study have given clear support to the provisional conclusions we sought to confirm. They have demonstrated unequivocally that smokers tend to have unhealthier lifestyles than non-smokers in very many respects and have also made

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it clear that indices of passive smoke exposure in the home are also markers of increased exposure to many other risk factors."

[5] **Tredaniel, J., Boffetta, P., Saracci, R., and Hirsch, A., "Exposure to Environmental Tobacco Smoke and Risk of Lung Cancer: The Epidemiological Evidence,"** ***European Respiratory Journal*** **7: 1877-1888, 1994 [Issue 87, Item 27]**

This fourth review by a team of IARC scientists reaches the conclusion that ETS exposure is causally related to the development of lung cancer in nonsmokers. It is based on a review of the epidemiologic studies published since 1986, and also discusses a number of additional forms of data, including references on confounding, biases and animal data.

EXCERPTS:

"Among the other health effects which have been associated with ETS exposure are other types of cancer, non-neoplastic respiratory diseases, acute respiratory illnesses and cardiovascular diseases. They have been reviewed extensively. The present review is restricted to lung cancer, and will focus mainly on a discussion of studies published since 1986."

"At the time that the report of the Surgeon General and other reports were compiled, information on ETS and lung cancer was available from 13 epidemiological studies."

"Eleven case-control studies were reviewed by either the 1986 report of the Surgeon General or the National Research Council report. Four further studies provided very limited information, and were not considered by these two reports, nor will they be discussed in detail here."

"At least 14 new case-controls [sic] studies have been published since those reviews. Seven further studies have also been published since 1987, but they are not reviewed in detail here because of major methodological limitations."

"The 14 recent case-control studies concentrated on ETS exposure through spousal smoking during adulthood. However, a growing number of studies have addressed other sources of ETS exposure, namely during childhood, from household members other than the husband, at work, and in other situations outside the home. Moreover, more sophisticated indices of ETS exposure have been used."

"It is highly unlikely that chance alone can explain the association between ETS and lung cancer. Even if the increase in risk seems to be no higher than 40%, the size of the populations which have been studied is large enough to exclude, with reasonable confidence that it originated only by random statistical variation. . . . However, most of the studies which we have reviewed, especially the early ones, although suggestive of a positive effect, have had several deficiencies, which could substantially bias their results and make their interpretation problematical."

"Of particular concern are former and current smokers who report themselves as nonsmokers, and, thus, may have been at higher risk for lung cancer than true nonsmokers, because of a history of smoking, rather than exposure to ETS. . . . Of particular concern, is the concordance of smoking habits in married couples: a woman who claims to be a nonsmoker is more likely to be, or to have been, an actual smoker if married to a smoker than if married to a nonsmoker. Conversely, misreporting among controls -- and unrecognized exposure due to a degree of background ETS -- tend to overstate the percentage classified as exposed to ETS. This artificially elevates the exposed percentage in controls relative to cases, thus, contributing to an underestimation of risk. A final possibility is that a nondifferential misclassification in the two groups leads to a point estimate that is biased towards the null value. It is plausible, that the first hypothesis is most commonly implied in the studies on ETS and lung cancer."

"The data available suggests a misclassification of smoking status is not likely to explain the excess risk."

"The lack of quantitative ETS exposure data in many epidemiological studies has also been questioned. However, the more recent studies have included, as far as possible, a quantitative or semiquantitative evaluation of ETS exposure from the spouse and other sources, during childhood as well as adulthood, and their results are consistent with previous studies."

"A more serious problem might be the misclassification of past smoking habits."

"Finally, one must stress that because there is widespread exposure to ETS, the upward bias on the relative risk of lung cancer caused by smoker misclassification is counterbalanced by the downward bias from background ETS exposure to the supposedly unexposed group."

"The existence of a differential in accuracy of obtaining ETS exposure histories between living and deceased subjects has been raised. . . . [F]rom the scarce evidence available, it does not seem that this type of bias can explain the positive results."

"A further factor that must be considered is recall bias, i.e. the possibility that a nonsmoking woman, or a

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respondent, with lung cancer will falsely inflate the ETS exposure from the spouse in an attempt to find a causal explanation for her disease."

"Two kinds of problem are to be discussed concerning the clinical and pathological diagnosis of lung cancer. Firstly, the fact that, in some studies, no histological verification exists that the patients were suffering from primary lung cancer."

"The second problem is the distinction between a primary neoplasm and metastases coming from an extrapulmonary cancer, as much as adenocarcinomas are the most frequent lung tumours in lifelong nonsmokers. However, a diagnosis of primary lung cancer in a lifelong nonsmoker is a fairly rare situation, which involves the physician in the search for a primary extrapulmonary tumour, such as breast cancer in females, since treatment and prognosis are very different. Moreover, if secondary tumours are not excluded from the case series, the RR associated with any factor that causes primary lung carcinomas are [sic] likely to be underestimated (unless the extrapulmonary cancer is associated with ETS exposure more strongly than lung cancer)."

"Publication bias has been questioned, in particular by Mantel, i.e. papers with nonsignificant or negative results are either not submitted or not accepted for publication in the scientific literature. However, publication bias can be active in either direction, i.e. the desire to minimize the impact of false positive assertions could result in a preference for publishing findings that refute a previous claim, rather than confirmatory results."

"Very few data are available on the possible confounding effect of risk factors for lung cancer other than ETS. . . . [A]ll recent studies have taken some possible confounding factors into account in multiple logistic analyses: age, ethnicity, diet, occupational exposures, education, income, religion and marital status have been examined."

"Diet may be an important confounder in studies of passive smoking and lung cancer. . . . Limited data are available to address this issue."

"[T]here is no convincing evidence that these potential confounding factors could have affected the results of these studies."

"In spite of the varying characteristics of each study, the three cohort studies, and 20 of the 23 case-control studies showed a weak positive association, with statistical significance being achieved in about half of the studies. The evidence remains statistically significant and conclusive after adjustments for smoker misclassification."

"In the case of ETS exposure, the proportion of adenocarcinomas is superior to that currently noted for male active smokers; whereas, adenocarcinoma is the most frequent cancer type in females. As ETS-related lung cancers occur mainly in females, the criterion for specificity is not completely fulfilled, excluding the fact that the proportion of adenocarcinomas in lung cancer of lifelong nonsmoking females is higher than that in current or former smokers."

"The fact that similar risk estimates have been found in populations which are genetically different, and are exposed to different environmental factors, argues in favour of a general association between ETS and lung cancer."

"Based on the firmly established causal association of lung cancer with active smoking, with a dose-response relationship down to low doses, passive smoking is considered likely to have a similar effect on the lung. . . . [T]hese dose-response studies have suggested the existence of a true and relatively consistent exposure-response relationship, especially when considering the level of smoking by the spouse, but a less consistent relationship with years of exposure."

"It is, therefore, biologically plausible that passive smoke exposure causes lung cancer, because of [the] presence of carcinogens to which there is no established lower threshold level of exposure for the development of lung cancer."

"There are no lifelong animal inhalation studies of ETS . . . New epidemiological studies in pet animals could add to the understanding of ETS effects in human populations."

"In the case of ETS and lung cancer, as the chemical components are the same as those of mainstream smoke, some of the effects of ETS must be analogous to those of active smoking. Thus, the risks observed at higher levels of exposure can be extrapolated at low doses."

"In summary, all the available data seem to fulfil at least to a reasonable degree, the criteria needed to accept a causal link between ETS and lung cancer among lifelong nonsmokers."

"The individual risk of lung cancer from exposure to ETS does not have to be very large to translate into a significant health hazard, because of the large number of smokers and the widespread presence of ETS. The size of this effect, in terms of numbers of lung cancers caused in different populations, is still a matter of research and debate."

"The causal relationship between ETS and lung cancer seems now to be clearly established. Even though ETS

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poses a lower risk than active smoking, it yields an appreciable number of deaths, because of the large number of potentially exposed individuals. On the assumption that the observed summary rate ratio of 1.3 for lung cancer is causal, the lifetime attributable fraction for lifelong nonsmokers has been calculated to be 390-900 per 100,000 deaths. The magnitude of this health risk in different settings, especially at work, must be more precisely calculated. However, enough is already known (in conjunction with data on active smoking) to justify action and the restriction or prohibition of smoking, especially in areas where tobacco consumption is still high, as in most European countries."

[6] Wynder, E.L., and Hoffmann, D., "Smoking and Lung Cancer: Scientific Challenges and Opportunities," *Cancer Research* 54: 5284-5295, 1994 [Issue 87, Item 28]

In this review of a number of issues related to active smoking and lung cancer, the authors also discuss data on ETS and lung cancer. They describe the epidemiologic data as "not conclusive," and suggest that a prospective epidemiologic study including biomarkers for exposure assessment would be necessary for a "conclusive evaluation" of the issue.

EXCERPTS:

"[S]everal key questions on smoking and lung cancer are still awaiting answers."

"In this overview we will discuss some of these unresolved issues. They include: (a) the change in the distribution of the major histological types of lung cancer during the past four decades, and a gender-related difference in the occurrence of squamous cell carcinoma and adenocarcinoma of the lung; (b) the differences in the lung cancer incidence rates between American and Japanese smokers and between African-American and White American male smokers; (c) the debated issues on the association between passive (involuntary) smoking and lung cancer; and (d) monitoring of cigarettes and smokers."

"In 1981 two separate reports linked ETS exposure with lung cancer in nonsmokers. In the following 12 years, 3 publications of additional cohort studies and 26 case-control studies have dealt with the association of exposure to ETS and lung cancer in nonsmokers. The majority of these publications reported a slight increase in lung cancer mortality for passively exposed nonsmokers compared to the controls. The earlier studies did not detect advanced histological changes in the lungs of nonsmokers. However, more recently in autopsy cases of nonsmokers who had been exposed to ETS during their lifetime, epithelial lesions in the lungs were seen more frequently than in the lungs of nonsmokers without ETS exposure; however, the difference was not statistically significant. These epithelial lesions are considered to be precursors of lung cancer, yet this aspect requires further detailed study."

"ETS is primarily a composite of the smoke generated between puffs, the SS, and a minor portion of mainstream smoke constituents that are exhaled after a smoker has taken a puff. Although per volume, undiluted SS contains more toxic and carcinogenic agents than mainstream smoke, the dilution of SS with air reduces this concentration rapidly. Nevertheless, appreciable levels of tobacco-specific ETS components have been detected in indoor air. . . . Nicotine and one of its major metabolites, cotinine, have been detected in physiological fluids, such as urine of nonsmokers, as a result of exposure to ETS. . . . The bladder carcinogen 4-amino-biphenyl, which transfers into ETS from tobacco smoke, has been detected as a hemoglobin adduct in involuntary smokers."

"[T]here is an apparent dichotomy between experimental data which support the concept that ETS gives rise to some risk of cancer, and epidemiological data, which are not conclusive in respect to ETS exposure and cancer."

"Since the publication of the International Agency for Research on Cancer report in 1985, about 30 additional epidemiological studies have been carried out. Each of these reported for exposed nonsmokers a risk for lung cancer of less than 2.0, relative to the risk of a nonsmoker without significant ETS exposure. This applies also to a multicenter population-based case-control study published in 1994. . . . As in all ETS-lung cancer studies in 'never-smokers,' assessment of their lifetime exposure remains problematic as long as reliable biomarkers of uptake are lacking."

"Perhaps the greatest uncertainty about the epidemiological data is due to the unreliable information obtained by questioning volunteers in regard to their smoking habits. This is exemplified by a large-scale study carried out in Southern Germany. . . . Among 800 ex-smokers who claimed to be nonsmokers 6.3, 6.5, and 5.2% had cotinine levels above 20 ng/ml during the three time periods. The percentages of self-proclaimed neversmokers who were actual smokers according to cotinine analyses were 0.5, 1.0, and 0.9%, respectively. Furthermore, 17.6% of formerly self-reported ex-smokers declared themselves later to be lifelong never-smokers."

"The limited reliability of data obtained by questionnaire, and the relatively limited number of nonsmokers

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with lung cancer who were not exposed to carcinogens in occupational settings, point to the need for a prospective epidemiological study with exposure assessment by biomarkers (e.g., cotinine and metabolites of polynuclear aromatic hydrocarbons and/or NNK in urine) to bring about a conclusive evaluation of the question on causality between involuntary smoking and lung cancer."

CARDIOVASCULAR ISSUES

[1] He, Y., Lam, T.H., Li, L.S., Du, R.Y., Jia, G.L., Huang, J.Y., and Zheng, J.S., "Passive Smoking Can Affect Blood Lipid Metabolism, Fibrinogen and Viscosity in 'Never Smoking' Women," *Atherosclerosis* 109(1,2): 20, 1994 [Issue 87, Item 29]

The authors of this abstract conclude that ETS exposure affects characteristics of the blood, and suggest that these changes might contribute to the causation of coronary heart disease.

EXCERPTS:

"The objective was to determine whether blood lipid profile, fibrinogen and viscosity are associated with passive smoking. . . . Exposure to passive smoking, obtained by standardized interviews, was defined as exposure from husband or co-workers or both for at least 5 years."

"59 subjects were not exposed to passive smoking and 98 were exposed."

"The results were similar after controlling for age, body mass index, medical history and other lipid levels."

"It is concluded that passive smoking can affect blood lipid metabolism, fibrinogen and viscosity in never smoking women and may contribute to the causation of coronary heart disease."

[2] Neufeld, E.J., Mietus-Snyder, M., Beiser, A., Baker, A., and Newburger, J.W., "Passive Smoking Is Associated with Reduced HDL-Cholesterol Levels in Children with High-Risk Lipid Profiles," *Circulation* 90(4 Part 2): I-102, 1994 [Issue 87, Item 30]

In this abstract, the authors conclude that children from homes with smokers had decreased levels of high density lipoprotein cholesterol. They suggest that this may contribute to an increased risk for atherosclerosis later in life.

EXCERPTS:

"We studied the relation of passive smoking to lipid profiles in 103 children and adolescents referred for dyslipidemia to a tertiary lipid referral center. Of these, 33 (32%) came from households with cigarette smokers. HDL-C levels were 38±6 mg/dl (mean±SD) in passive smokers vs 44±10 mg/dl in children without smoke exposure. Smoking exposure was not significantly associated with total cholesterol, LDL-C, or triglyceride levels. In addition to passive smoking, HDL-C levels were significantly correlated with dietary fat intake, and inversely related to body mass index (BMI), and serum triglyceride levels. The magnitude of passive smoking effect on HDL-C was minimally affected in models including potential confounders such as triglyceride level, and dietary fat tertiles. In multivariate regression adjusting for BMI, age, exercise and dietary fat, passive smoking remained a significant risk factor for decreased HDL-C."

"We conclude that passive smoking may worsen the risk profile for later atherosclerosis among high-risk young persons."

[3] Penn, A., Chen, L.-C., and Snyder, C.A., "Inhalation of Steady-State Sidestream Smoke from One Cigarette Promotes Arteriosclerotic Plaque Development," *Circulation* 90: 1363-1367, 1994 [Issue 87, Item 31]

In the second report on the experimental induction of arteriosclerosis in cockerels (young male chickens) exposed to sidestream smoke, the authors conclude that, at levels comparable to those found in "smoke-filled environments," sidestream smoke exposure increases the size of arteriosclerotic plaques.

EXCERPTS:

"[T]hree surrogates -- carbon monoxide, total suspended particulates, and nicotine -- are measured routinely to provide estimates of the amount of sidestream smoke that is generated. . . . In our initial study, relatively high steady-state levels of these surrogates were measured in the smoke exposure chambers. The relevance of these levels to those reportedly encountered in environmental situations is the subject of some debate."

"In the present study, we lowered the smoke exposures by a factor of 5. Cockerels were exposed to the sidestream smoke from the steady-state combustion of 1 cigarette. The timing and duration of exposure were the same as in the first series of studies. Plaque sizes were again significantly larger in the sidestream smoke-exposed group than in controls, although the magnitude of the size increase was lower than in the 5-cigarette study. The environmental relevance of this study is highlighted by independent measurements of carbon monoxide levels that were made in commercial establishments where cigarette smoking

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was taking place. In four of four cases, steady-state carbon monoxide levels equaled or exceeded the carbon monoxide levels measured in the smoke exposure chambers during the 1-cigarette study."

"Carbon monoxide levels averaged 4.33 ppm in the four chambers, suspended particulates averaged 2.48 mg/m^3, and nicotine values averaged 108.3 ug/m^3."

"Microscopic plaques were present in the abdominal aortas of all cockerels in each group. Neither the number of plaques per cockerel nor the mean number of plaque-containing aortic segments per cockerel was significantly different in the two groups. There were 63 of 100 (63%) plaque-containing abdominal aorta segments from control cockerels and 200 of 295 (68%) plaque-containing aortic segments from sidestream smoke-exposed cockerels."

"Although inhalation of the steady-state sidestream smoke from 1 cigarette had no effect on plaque numbers or on their spatial distribution, it did result in a measurable increase in plaque sizes. The average plaque index values on a segment-by-segment basis for all cockerels in both groups are presented. For each of the 10 sets of segments in the 10 controls, 3 to 8 samples had plaques. For each of the 10 sets of segments in the 30 smoke-exposed cockerels, 12 to 26 segments had plaques."

"[W]e sought an objective assessment of the relation of exposure-chamber smoke surrogate measurements to the doses of environmental tobacco smoke to which people can be exposed routinely. We measured carbon monoxide levels for periods ranging from 60 to 180 minutes in a series of establishments where cigarettes were being smoked."

"[P]eople in enclosed public areas where secondhand cigarette smoke is being generated can be exposed to carbon monoxide levels that equal or exceed the levels we measured in the cockerel exposure chambers during the present secondhand smoke study."

"Whether inhalation of environmental tobacco smoke results directly in quantifiable, deleterious health effects has been the subject of some controversy."

"The cockerel is a particularly appropriate model for plaque acceleration studies. It is well established that the fibromuscular abdominal aorta plaques in the cockerel are very similar histologically and ultrastructurally to fibrous coronary artery plaques in humans. The standard chow diet fed to the cockerels is low in cholesterol and saturated fat. The plaques that appear in the abdominal aorta have little lipid involvement. However, if the diets are supplemented with 1% cholesterol, plaque sizes increase by more than a factor of 2. Whether these animals ingest cholesterol as a diet supplement, receive carcinogens by injection, or inhale cigarette smoke, the result is the same: accelerated development of arteriosclerotic plaques. The effect of these exposures is to increase the size of microscopic plaques to the point where many become visible to the naked eye. There are no significant increases in the actual numbers of plaques and no differences in areas within the aorta where plaques originate compared with control values."

"These findings may have important public health implications. . . . [S]moking acts primarily to promote development of arteriosclerotic plaques that already exist. The results here combined with those from the previous 5-cigarette study support this view and demonstrate that involuntary exposure to secondhand smoke at levels equal to or even lower than those found in routinely encountered smoking environments will accelerate arteriosclerotic plaque development. The effect may be especially pronounced, and largely avoidable, in young children. We have not determined yet whether the smoke-associated plaque size increases in cockerels are reversible."

[4] **Sun, Y.-P., Zhu, B.-Q., Sievers, R.E., Glantz, S.A., and Parmley, W.W., "Metoprolol Does Not Attenuate Atherosclerosis in Lipid-Fed Rabbits Exposed to Environmental Tobacco Smoke," *Circulation* 89: 2260-2265, 1994 [Issue 82, Item 31]**

The authors of this study report that a beta-blocker, metoprolol, while decreasing the development of atherosclerotic lesions in rabbits fed a high-fat diet, did not "protect against the effects" of ETS, which was claimed to increase the development of those lesions.

EXCERPTS:

"We previously demonstrated that exposure to environmental tobacco smoke (ETS) increases the development of atherosclerosis in lipid-fed rabbits. Clinical studies have suggested a protective effect of beta-blockers in smokers. Accordingly, we evaluated the effects of metoprolol in this animal model to see whether this beta-blocker would block the atherogenic effects of ETS."

"Thirty-two New Zealand White male rabbits on a 0.3% cholesterol diet were randomly divided into four groups: ETS-metoprolol (ETS-M), ETS-control (ETS-C), and non-ETS with metoprolol (NETS-M) and without metoprolol (NETS-C). . . . Rabbits in the ETS groups were exposed to sidestream smoke from four Marlboro cigarettes per 15 minutes, 6 hours a day, for 10 weeks. Average air carbon monoxide (CO), nicotine, and total particulates (TP) in the exposure chambers were 67.2±3.1

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(SEM) ppm, 1133.7±78.4 ug/m^3, and 37.7±3.0 mg/m^3, respectively."

"The rabbits exposed to ETS had significantly higher levels of lipid deposits in their arteries (average lipid deposits of the aorta and pulmonary artery, 37±1% for controls versus 53±1% for ETS-exposed rabbits), with higher levels in the aorta than the pulmonary artery. Metoprolol also significantly reduced the amount of lipid deposits (51±1% for controls versus 38±1% for metoprolol- treated rabbits, but this benefit was independent of whether the rabbits were exposed to ETS."

"We tested the hypothesis that ETS induces atherosclerosis by stimulating the beta-adrenergic system by giving metoprolol to lipid-fed rabbits exposed to ETS for 10 weeks. . . . Although metoprolol inhibited atherosclerosis in all groups, it did not significantly decrease the additional atherosclerosis caused by ETS in these rabbits. Thus, the beta-adrenergic system does not seem to be the key in ETS-induced atherosclerosis."

"Although there were no significant differences in plasma catecholamines in the study, it is clear that ETS can stimulate sympathetic activation. Short periods of sympathetic activation may cause disturbances of endothelial integrity and platelet function, both of which are key atherogenic processes. Repeated sympathetic activation may therefore contribute to acceleration of atherosclerosis."

"We conclude that the beta$_1$-adrenergic receptor antagonist metoprolol significantly reduced the development of atherosclerosis in lipid-fed rabbits. However, no additional protective effective on atherosclerosis induced by ETS was demonstrated. Thus, the beta$_1$-adrenergic receptor system is probably not the mechanism by which ETS induces atherosclerosis in rabbits."

Respiratory Diseases and Conditions —Adults

[1] **Bascom, R.A., and Fitzgerald, T.K., "A Vasoconstrictor Partially Alters the Nasal Response to Sidestream Tobacco Smoke,"** ***American Journal of Respiratory and Critical Care Medicine*** **Suppl. 149(4): A391 [Issue 86, Item 29]**

Nasal congestion and headache are the endpoints measured in this experiment, which reports a decrease in nasal symptoms reportedly due to ETS following use of a vasoconstrictor.

Excerpts:

"Upper respiratory symptoms following environmental tobacco smoke exposure are common but their pharmacologic modulation has not been studied. The purpose of this study was to examine the hypothesis that pretreatment with an alpha adrenergic vasoconstrictor would block the nasal congestion and symptoms associated with controlled exposure to sidestream tobacco smoke (SS). Eight healthy nonsmoking young women . . . were exposed on three separate days. . . . Subjects recorded symptoms of nasal congestion and headache and underwent measurement of nasal resistance (NAR) by posterior rhinomanometry and mid-nasal volume by acoustic rhinometry before, during and following the smoke exposure. . . . In conclusion, pretreatment with a topical alpha adrenergic vasoconstrictor blocks increased nasal resistance and anterior nasal volume (data not shown), partially blocks the symptom of nasal congestion, but does not reduce headache or alter the reduction in mid nasal volume associated with SS exposure."

[2] **Frette, C., Edelstein, S., Clausen, J., Barrett-Connor, E., "Effects of Active and Passive Smoking on Lung Function in Elderly Men and Women,"** ***American Journal of Respiratory and Critical Care Medicine*** **Suppl. 149(4): A393, 1994 [Issue 86, Item 30]**

The authors of this abstract report no statistically significant effect of ETS exposure on lung function in a cohort of elderly persons.

Excerpts:

"There have been few population-based studies assessing pulmonary function in the elderly. We examined the relation of active and passive cigarette smoking on lung function in a population-based sample of older adults. Between 1972 and 1974, a population survey was conducted in the community of Rancho Bernardo, a geographically-defined predominantly white upper-middle class community; 82% participated. from 1988 to 1991, 80% of surviving local subjects had pulmonary function assessed by spirometry using standard ATS criteria. There were 571 men aged 54-94 and 826 women aged 51-95. Age-and height-adjusted FEV1 was significantly lower in current smokers than in nonsmokers among both men and women. among past-smokers, adjusted FEV1 decreased significantly with increasing age at quitting in both men and women. Adjusted FEV1 was similar in past smokers who quite before age 40 years than in never-smokers among both men and women. OF the 176 never smoking men, 103 were exposed to their spouse's smoke and of the 415 never smoking women, 310 were exposed

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to their spouse's smoke; adjusted FEV1 was similar to both men and women exposed to passive smoke compared to never smokers. . . . Among never smokers, the decrease of FEV1 with age was nonsignificantly higher in those with passive smoke exposure than in those without, with regression coefficients of FEV1 on age. . . . These results confirm the deleterious effect of active smoking on lung function in elderly adults and the beneficial effect of quitting. No significant effect of passive smoking on lung function was observed in this elderly cohort."

[3] Jindal, S.K., Gupta, D., and Singh, A., "Indices of Morbidity and Control of Asthma in Adult Patients Exposed to Environmental Tobacco Smoke," *Chest* 106: 746-749, 1994 [Issue 84, Item 27]

The authors of this study, conducted in India, report that ETS-exposed asthmatics required more medication, had more emergency room visits, had more acute episodes of asthma, and were absent from work more often than were controls, who had asthma but were not exposed to ETS.

EXCERPTS:

"The study was undertaken to compare the indices of morbidity and control of asthma in 100 adult patients exposed to environmental tobacco smoke (ETS) inhalation (group 2), with 100 asthmatics not exposed (group 1). Exposure was established from the history of smoking by the patient's spouse and other close contacts. Asthma control and morbidity were assessed during their follow-up visits in the chest outpatient clinic by inquiring into the emergency department (ED) visits, hospitalization, acute episodes, requirement of parenteral drugs at home, corticosteroids, and maintenance bronchodilators in the preceding 1-year period. . . . Lung function was recorded."

"While mean VC was almost similar, the forced expiratory flows such as FEV_1 and FEF25-75% were lower in group 2 than in group 1 patients."

"The number of patients with acute episodes and complications of asthma were [sic] similar in the two groups. The number of patients who were absent from work because of their illness were [sic] similar, but the duration of absence, expressed in weeks per patient, was longer in the ETS-exposed group."

"Most other indices, when expressed per patient per year, were significantly higher among the ETS-exposed group. These included the numbers of visits to the hospital ED, acute episodes, and parenteral bronchodilator injections at home."

"The present study has shown an increased morbidity in the ETS-exposed patients with asthma, as assessed by the number of visits to the ED, acute episodes, administration of parenteral bronchodilators at home, weeks of corticosteroid requirement, and duration of absence from work. The number of patients with increased asthma morbidity was similar in the two groups. However, the patients with greater severity in the ETS-exposed group required a greater amount of maintenance bronchodilators and corticosteroids for control of their symptoms. This is further corroborated by the presence of poorer forced expiratory flows during the period of stability despite an increased drug requirement in the ETS-exposed patients."

[4] Kuenzli, N., Schwartz, J., Leuenberger, P., Ackermann-Liebrich, U., and the SAPALDIA Team, "Association of Environmental Tobacco Smoke at Work and Forced Expiratory Lung Function," *American Journal of Respiratory and Critical Care Medicine* Suppl. 149(4) Part 2: A393, 1994 [Issue 87, Item 32]

The authors of this abstract conclude that workplace ETS exposure is associated with decreased lung function in asthmatic women.

EXCERPTS:

"The relationship of passive smoking exposure at work place (ETS) and lung function was examined in a subsample of the SAPALDIA cross-sectional study, a population based random sample across eight Swiss areas. In total, all 3300 lifetime never smokers, 18-60 years of age, with acceptable forced expiratory lung function assessment were included in the analysis."

"Logarithms of FEV1 and FEF25-75% were separately used as dependent variables. ETS was defined as tobacco smoke exposure at work derived from questionnaire data."

"Females reporting ETS exposure at work had a significant 8% lower adjusted mean FEV1 and 18% lower FEF25-75% than nonexposed. In the other subgroups no clear relationship was detected. Adjustment for an individual ETS annoyance score did not change the results."

"Lower lung function in asthmatic female but not male was associated with ETS at work. Quality and quantity of ETS exposure at work might differ by gender. Using number of persons to or hours per day exposed to any ETS we observed a significant dose-response. Furthermore ETS at work was a significant predictor for actual medication in asthmatic females. Overall the data do not contradict a causal relationship of ETS at work and lung function, at least in susceptible subgroups, after controlling for potential confounders, supporting the public health efforts for smoking free environments at work places."

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[5] **Ng, T.P., and Tan, W.C., "Epidemiology of Allergic Rhinitis and Its Associated Risk Factors in Singapore," *International Journal of Epidemiology* 23(3): 553-558, 1994 [Issue 83, Item 28]**

The authors of this study conducted in Singapore report that cockroach infestation, occupational exposures, and outdoor air pollution were among the factors associated with an increased risk of allergic rhinitis. They also report that ETS exposure was not statistically significantly associated with an increased risk of rhinitis.

EXCERPTS:

"Allergic rhinitis is characterized clinically by the presence of chronic or persistent nasal blockage, discharge, sneezing or itching, usually accompanied by conjunctivitis, which is provoked by various aeroallergenic exposures such as tree or grass pollens, house dust, animal danders, moulds, medicines, etc."

"In this study, various demographic and environmental determinants of allergic rhinitis were examined by analyzing data collected from a population study of respiratory diseases in Singapore."

"Questions on environmental risk factors included current keeping of dogs or cats, and birds; cockroach infestation in the home; use of rugs or carpets, of incense or mosquito coils; active smoking, passive exposure to tobacco smoke; occupational exposure to fumes, smoke or dust; outdoor air pollution; and heavy cooking fumes from the kitchen."

"A number of environmental factors showed statistically significant and highly elevated relative risks that suggest important associations with allergic rhinitis. These were cockroach infestations in the home, occupational exposure (to dust, fumes or gases), past smoking habit, and a high frequency of heavy cooking fumes from the kitchen. Several other factors such as keeping dogs, cats, or birds, having rugs or carpets, and passive exposure to tobacco smoke, also appeared to be associated with allergic rhinitis, but the estimated relative risks were less than 1.5 or were not statistically significant. No apparent association with use of mosquito coils and incense were [sic] observed."

"A weakness in the study is that self-reporting of symptoms and certain exposures may lead to biased observations of association. This is especially true for environmental variables such as the subjects' perception of occupational exposures and cooking fumes. Significant results observed for these exposures should therefore be interpreted with some caution. . . . [A] true association with rugs and carpets or pet ownership may not be detected by current ownership or use if people with allergic rhinitis gave up keeping pets, or having rugs and carpets, and if past exposures are more relevant than current exposures."

"The geographical variation in rates of allergic rhinitis among residential areas was likely to be explained by environmental or social influences, including aerobiological exposure to plant or animal allergens."

[6] **Ostro, B.D., Lipsett, M.J., Mann, J.K., Wiener, M.B., and Selner, J., "Indoor Air Pollution and Asthma: Results from a Panel Study," *American Journal of Respiratory and Critical Care Medicine* 149: 1400-1406, 1994 [Issue 82, Item 32]**

Based on data collected on adult asthmatics in Denver, Colorado, the authors report statistically significant associations between use of a gas stove, wood smoke exposure or ETS exposure and several indices of asthma.

EXCERPTS:

"Although there is abundant clinical evidence of asthmatic responses to indoor aeroallergens, the symptomatic impacts of other common indoor air pollutants from gas stoves, fireplaces, and environmental tobacco smoke have been less well characterized. These combustion sources produce a complex mixture of pollutants, many of which are respiratory irritants. We report here results of an analysis of associations between indoor pollution and several outcomes of respiratory morbidity in a population of adult asthmatics residing in the Denver, Colorado, metropolitan area. A panel of 164 asthmatics recorded in a daily diary the occurrence of several respiratory symptoms, nocturnal asthma, medication use, and restrictions in activity, as well as the use of gas stoves, wood stoves, or fireplaces, and exposure to environmental tobacco smoke."

"Of the indoor sources, gas stove use was most strongly associated with moderate or severe cough (OR, 2.08; 95% CI, 1.77-2.44) and moderate or severe shortness of breath (OR, 1.89; 95% CI, 1.61-2.21). The use of a wood stove or fireplace was associated with both cough (OR, 1.44; 95% CI, 1.05-1.99) and shortness of breath (OR, 1.70; 95% CI, 1.24-2.31)."

"Exposure to domestic environmental tobacco smoke and to occupational irritants also exhibited statistically significant associations with both moderate cough and shortness of breath."

"The results of this analysis suggest that both outdoor air pollution and indoor sources of combustion can

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exacerbate asthma and cause several adverse health outcomes in a population of adult asthmatics."

"[I]t is of particular interest to examine the effects in asthmatics related to daily exposures. In some cases, exposures to these indoor sources almost doubled the odds of experiencing several of the adverse health outcomes."

"To our knowledge, our analysis is the first empirical demonstration of the effect of wood smoke on daily symptoms in adult asthmatics."

"This investigation documents a strong daily relationship between exposure to cigarette smoke and increased probabilities of clinically significant symptoms in free-living asthmatic adults. As such, it supports previous studies linking exposure to smoke and asthma exacerbations. Our analysis probably underestimates the total effect of environmental tobacco smoke since the daily diary did not distinguish among the occupational exposures to 'smoke, dust, or fumes.' It is likely that environmental tobacco smoke constituted some, if not most, of the occupational exposures associated with adverse outcomes in this study population."

"The principal public health implication of our findings is that those with moderate to severe asthma should reduce to a minimum their exposure to residential sources of combustion, including gas stoves, tobacco smoke, and fireplaces or wood stoves. Exposure to these indoor sources of air pollution may result in exacerbations of various asthma symptoms and nocturnal asthma, physician or emergency room visits, and restricted activity. Whether these effects would occur in persons with mild asthma or other respiratory illness should be addressed by future research."

[7] Samet, J.M., "Learning About Air Pollution and Asthma," *American Journal of Respiratory and Critical Care Medicine* 149: 1398-1399, 1994 [Issue 82, Item 33]

In an editorial accompanying the Ostro, et al., study, Samet suggests that the data of the study support a suggested causal relationship between ETS exposure and asthma, and suggests that other reported associations, e.g., with wood smoke, be interpreted "more cautiously."

EXCERPTS:

"[T]he findings led the authors to conclude that respiratory irritants produced by domestic combustion increase morbidity in asthmatics and that asthmatics should minimize exposures to residential sources of combustion."

"Are this conclusion and the related recommendation warranted? Associations between exposures and outcomes identified in observational data may reflect chance, bias, or cause. Significance testing provides an indication of the probability that associations reflect chance. In the study by Ostro and colleagues, most associations achieve significance, although the level of significance declined in the analyses based on the generalized estimating equation method. Nonetheless, the associations are of a magnitude of potential public health significance. Could they reflect the bias? Ostro and colleagues controlled bias from confounding, the mingling of the effect of one variable with that of another, using multivariate statistical approaches."

"Should the associations be considered causal? . . . The findings of the study by Ostro and colleagues provide additional confirmation of the adverse effect of tobacco smoke on asthmatics. The associations with two other sources of combustion emissions, gas stoves and wood stoves or fireplaces, should be interpreted more cautiously."

"On the other hand, a general recommendation that persons with asthma should reduce exposures to combustion emissions is consistent with recommendations of the National Asthma Education Program and established clinical practice. It is likely that persons with more severe asthma do voluntarily limit such exposures, as suggested by the low prevalence of exposure (9%) to tobacco smoke reported by the subjects in the study by Ostro and coworkers."

[8] Xu, X., Lee, B., and Wang, L., "Exposure-Response Relationship Between Passive Smoking and Pulmonary Function in Adults," *American Journal of Respiratory and Critical Care Medicine* Suppl. 149(4) Pt. 2: A393, 1994 [Issue 87, Item 33]

This abstract claims that, in a population of residents of Beijing, China, there is a "dose-dependent" association between ETS exposure and reduced lung function.

EXCERPTS:

"The effects of exposure to environmental tobacco smoking (ETS) on pulmonary function were investigated in a random sample of 1.033 adults aged 40 to 69 yrs from a residential area in Beijing. 310 reported exposure to ETS both at home and at workplace; 242 at home only; 277 at workplace only; and 204 neither at home nor at workplace. The average living area was small (about 26 m^2 per household) compared to USA, implying higher ETS concentration for given number of cigarette[s] smoked. ETS exposures were considered as both a

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categorical and a continuous variable. Regression methods were used to quantify the effects of ETS, adjusting for sex, age, height, educational level, annual family income, indoor use of coal stoves for heating and for cooking, occupational exposure to dusts, gases or fumes, active smoking (total years, types, and current smoking status), interactions between sex and smoking, and height, and between exposure to ETS at home and at workplace. Compared to those not exposed, those exposed to ETS either at home or at workplace were associated with 102 ml reduction in FEV_1 and 151 ml reduction in FVC. Using separate indicators for ETS exposure at home versus workplace, the former was associated with 102 ml reduction in FEV_1 and 105 ml reduction in FVC; and the [latter] was associated with 61 ml reduction in FEV_1 and 80 ml reduction in FVC. When the subjects were grouped into three exposure categories (none, home only or workplace only, and both), the deficits in FEV_1 and FVC in 'both' group were the greatest and statistically significant. The adverse effects of ETS were consistently observed in both sexes, in both never-smokers and smokers, and in all the occupational strata. When ETS exposure was measured by the number of cigarettes smoked by other household members at home per day, an exposure-response relationship between ETS exposure and FEV_1 and FVC was clearly indicated. A test of the linear tend was statistically significant in both men and women, in smokers, and in male never-smokers. In conclusion, this study demonstrated that there is a significant association between exposure to ETS and reduced level of FEV_1 and FVC in adults, and such an association is dose-dependent."

Respiratory Diseases and Conditions —Children

[1] **Agudo, A., Bardagi, S., Romero, P.V., and Gonzalez, C.A., "Exercise-Induced Airways Narrowing and Exposure to Environmental Tobacco Smoke in Schoolchildren,"** ***American Journal of Epidemiology*** **140(5): 409-417, 1994 [Issue 84, Item 28]**

Maternal smoking was reportedly associated with an increased risk of exercise-induced airways narrowing, a symptom of bronchial hyperresponsiveness, in the sample of asthmatic Spanish children studied in this case-control study.

Excerpts:

"Bronchial hyperresponsiveness is an exaggerated response of airways that is induced by nonsensitizing bronchoconstrictive stimuli, and exercise-induced airways narrowing (EIAN) is a common feature in the asthmatic child."

"[W]e carried out a case-control study, the main objective being to assess the association between EIAN and environmental tobacco smoke in children."

"In 1990 a cross-sectional study was carried out on a random sample of 2,056 schoolchildren aged 9-14 years, residing in Mataro, Spain. A test was performed measuring the peak expiratory flow rate at rest and postexercise. A decrease in the peak expiratory flow rate of ≥15 percent was considered a positive test of EIAN."

"The environmental tobacco smoke exposure at home was recorded as a detailed description of the smoking habits of both parents and any other person who had lived in the same house for at least 6 months. For each person smoking at home, the following variables were recorded: the type of tobacco, the total amount smoked per day, and the specific amount smoked at home, taking into account the differences between weekdays and weekend. Information about exposure in vehicles and public places included the type of vehicle and the mean time spent per week, separately for weekends and weekdays. For each source, information was collected from the child's birth until the time of the interview."

"When each source was considered without taking into account other sources, only the exposure from the mother presented a significant odds ratio. . . . The risk of exposure from the mother, compared with those never exposed from the mother, remained significant after adjusting for other sources of exposure in the home (odds ratio = 1.91, 95 percent confidence interval 1.08-3.41)."

"Regarding the duration, intensity, and cumulative exposure, there is an overall tendency for the more heavily exposed to be at greater risk. There seems to be a higher risk for children exposed since birth than for those whose exposure started after the first year of life. Among other sources of environmental tobacco smoke exposure, only the exposure in vehicles for >9 years and for >30 minutes per week presented a high (but not significant) odds ratio."

"According to our results, environmental tobacco smoke exposure may be considered as a factor associated with the occurrence of EIAN in children. . . . A major drawback of working with prevalent instead of incident cases is the uncertainty of causal inference. We cannot be sure that

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the exposure took place before the onset of the condition. However, we have recorded a complete history of exposure, and the association was consistently found in different periods of time."

"Results of our study reinforce the hypothesis that environmental tobacco smoke has a role in the development of bronchial hyperresponsiveness in children. The only relevant source of environmental tobacco smoke exposure at home seems to be from the mother. The reasons for this are unclear, but the proximity between mother and child could explain it. Therefore, several points remain to be clarified in future studies, the prenatal and postnatal effects of smoking and the interaction between atopy and environmental tobacco smoke exposure being, in our opinion, the most important."

[2] Brabin, B., Smith, M., Milligan, P., Benjamin, C., Dunne, E., and Pearson, M., "Respiratory Morbidity in Merseyside Schoolchildren Exposed to Coal Dust and Air Pollution," *Archives of Disease in Childhood* 70: 305-312, 1994 [Issue 83, Item 29]

Based on a study of children in several neighborhoods in Liverpool, England, the authors report that respiratory symptoms were more prevalent in those children exposed to coal dust. The authors also note that children of smokers had an increased symptom prevalence.

EXCERPTS:

"A cross sectional study was carried out to determine whether schoolchildren in a specific locality exposed to pollution from steam coal dust have an excess of respiratory symptoms compared with children in control areas."

"The study questionnaire includes questions on several factors related to the risk of asthma. These include: type of dwelling (construction, carpets, dampness); type of heating; furred pets in the house currently and previously; parent smoking at the time of the study and previously; type of infant feeding; and family history of allergy. This allows risk factors for respiratory morbidity other than air pollution to be assessed."

"There were significant socioeconomic differences between the exposed and control zones. Parental unemployment, the proportion of housing that was rented or was damp, and the proportion of smoking parents were all significantly higher in the exposed area."

"[T]here was a significantly increased prevalence of most of the respiratory symptoms in the exposed group. Thus in the exposed zone significantly more children had been diagnosed by a doctor as having asthma and their asthma was less likely to be well controlled. In contrast, factors known to predispose to asthma, such as one or both parents having asthma or the presence of any allergy, were not higher in the exposed area."

"For each of the socioeconomic differences between the areas the groups were divided into two strata for that variable and the between group comparisons repeated. . . . Children of smokers do have more respiratory symptoms than the children of non-smokers, but for both smoking and non-smoking subgroups there remains an increased incidence of respiratory symptoms in the area exposed to dust. This pattern of exposed versus control group differences was consistent for each of these analyses."

"[A]lthough we can confidently state that there is a respiratory problem in the exposed area, we cannot attribute the problem to a specific cause. There is an increased dust pollution problem in the area which is relatively recent and which provides a simple, straightforward explanation. Moreover, the effect on cough in particular fits with the hypothesis that this is the result of an increased burden of inhaled dust. Further studies are needed to confirm or deny the connection."

[3] Chen, Y., "Environmental Tobacco Smoke, Low Birth Weight, and Hospitalization for Respiratory Disease," *American Journal of Respiratory and Critical Care Medicine* 150: 54-58, 1994 [Issue 84, Item 29]

This Shanghai study included more than 3,000 infants; low birth weight and normal birth weight infants were compared. The author reports that among low birth weight infants, hospitalization became increasingly more likely with more smoking by household members.

EXCERPTS:

"Low birth weight (LBW) is a major determinant of infant mortality and morbidity. . . . This analysis focuses on the relationship between smoking habits of household members and hospitalization for respiratory disease in LBW infants."

"This analysis was performed on the combined data from the Jing-An and Chang-Ning Epidemiologic Studies of Children's Health in Shanghai."

"Both studies have shown that smoking status of household members was significantly related to hospitalization for respiratory disease. . . . The LBW infants had significantly higher risk of hospitalization for respiratory disease than the NBW [normal birth weight] infants."

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"[B]oth risk and incidence density of hospitalization for respiratory disease during the children's first 18 mo of life increased with increasing smoking consumption by household members among the LBW infants more rapidly than among the NBW infants."

"Educational levels of father and mother, mother's age at child's birth, monthly income per capita, number of household members, average living space per capita, cooking fuel, and adult diagnoses of COPD or respiratory disease were found either not to be associated with the outcome or not to substantially change the relationship between birth weight, ETS exposure, and the outcome."

"Certain limitations of this study need to be considered. First, the exposure assessment in this study and the study by Deng and coworkers did not include an objective measure of maternal smoking. A societal proscription against young women smoking in Shanghai might also result in underreporting of smoking by those young women. Maternal smoking during pregnancy could lead to both low birth weight and lower pulmonary function which might predispose the infants to respiratory hospitalizations. This bias could be substantial in this analysis, particularly if maternal smoking during pregnancy occurred in the 21 LBW infants from smoking households who were hospitalized for respiratory disease."

"Many factors are related to the actual amount of household exposure to ETS, including the number of cigarettes smoked in the house, household ventilation, the volume of enclosed space, time spent indoors, and the degree of contact between the infants and adult smokers. Shanghai is a crowded city. This study found that the average residential area per capita was only 5 sq m. The household size was about five persons on average."

"LBW modified the effect of ETS exposure on hospitalization for respiratory disease in that ETS exposure had a greater effect in the LBW infants. This analysis suggests that LBW infants are more susceptible to household exposure to ETS. LBW is related to prematurity. Increased influence of ETS exposure on hospitalization for respiratory disease in LBW infants may result from the retardation of lung growth."

[4] **Crain, E.F., Weiss, K.B., Bijur, P.E., Hersh, M., Westbrook, L., and Stein, R.E.K., "An Estimate of the Prevalence of Asthma and Wheezing Among Inner-City Children,"** *Pediatrics* **94(3): 356-362, 1994 [Issue 85, Item 26]**

Although smoking is not discussed in this study, the authors report a high prevalence of asthma among inner-city children, and suggest a relationship between incidence and factors related to ethnicity and income.

EXCERPTS:

"The purpose of this study was to determine the prevalence of reported asthma and wheezing in the Bronx, NY, an inner-city environment with previously reported high asthma morbidity and mortality."

"The asthma period prevalence rate among children in the Bronx RDD sample was twice that of US children."

"Within the Bronx, the association of poverty and asthma prevalence is most notable within the Hispanic population. The prevalence of active asthma among Hispanic children in the bronx, who are primarily Puerto Rican, is 10.0%, similar to the 11.2% rate found in Puerto Rican subjects from analysis of the 1982 through 1984 HHANES. In the Bronx Hispanic sample, income had a significant relationship to period prevalence that ranged from nearly 13% among the poorest Hispanics to 5.5% of those with household incomes of $30,000 or more."

"The nearly identical prevalence of asthma among boys and girls 0 to 11 years of age is surprising because most published studies have found that among young children, asthma is more prevalent among boys. Factors associated with living in the inner city may overcome differences in prevalence related to sex."

"This study supports the notion that poverty and race/ethnicity are associated with the prevalence of asthma, but it also suggests that the urban environment itself contributes to asthma prevalence. Although poverty alone, irrespective of the urban environment, may help to explain possible excessive exposure to indoor and outdoor allergens, poverty within an inner-city environment may provide uniquely higher exposures to certain aeroallergens or irritant gases. The crowding that accompanies urban poverty may lead to increases in viral respiratory illness that may be associated with the later development of asthma, or lead to exacerbations of acute illness in children with asthma."

[5] **Cunningham, J., Dockery, D.W., and Speizer, F.E., "Maternal Smoking During Pregnancy as a Predictor of Lung Function in Children,"** *American Journal of Epidemiology* **139: 1139-1152, 1994 [Issue 82, Item 34]**

Using data collected from over 8,000 North American children, the authors concluded that lung function decrements observed at age 8 to age 12 were associated with maternal smoking during pregnancy. They report

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that current maternal smoking was not associated with significant differences in lung function measurements.

EXCERPTS:

"This study examined the relative magnitude of the effects of maternal smoking during pregnancy and later childhood environmental tobacco smoke exposure on the lung function of 8- to 12-year-old children."

"Each child's history of environmental tobacco smoke exposure was assessed from information provided by the parent or guardian on the health questionnaire. Respondents were asked whether the child's mother smoked while she was pregnant with the child and, if so, during which trimester(s). No information was available on the mother's exposure to other people's smoke during pregnancy. The child's current exposure to environmental tobacco smoke was assessed from reported smoking in the home by the respondent, by a second primary adult, and by others, including regular visitors, with all questions referring to smoking in the year prior to the administration of the questionnaire."

"The estimated deficits in lung function associated with maternal smoking during pregnancy decreased only slightly after controlling for recent exposure and remained highly significant. The estimates for the effect of current environmental tobacco smoke exposure from maternal smoking were greatly reduced after controlling for prenatal exposure, however, and were no longer statistically significant."

"Controlling for current smoking in the home by the father (or other primary adult) and others did not substantially change the size of any estimate. In addition, there was no consistent evidence of an association between current paternal smoking or current smoking by others in the home and the lung function of children, even for children of never-smoking mothers (n = 5,326)."

"A persistent deficit in lung function that was associated with maternal smoking during pregnancy and that was not explained by current maternal smoking alone was observed in the children. The effects were observed primarily in measures of flow rather than volume, suggesting that changes involve the obstruction of airways. Exposure to maternal smoking in utero is qualitatively different from postnatal environmental tobacco smoke exposure. Prenatal exposure to maternal smoking is restricted to those components of mainstream smoke inhaled by the mother that eventually cross the placenta."

"Environmental tobacco smoke exposure during childhood, on the other hand, results from the combination of sidestream smoke and smoker-exhaled mainstream smoke, which may act directly on the respiratory system. Thus, the health effects associated with in utero environmental tobacco smoke exposure may be attributable to a different component of tobacco smoke than those associated with later, postnatal environmental tobacco smoke exposures. While specific mechanisms are not clear, it is important to note that the full complement of airways are present before the end of pregnancy, while alveolar proliferation continues until long after birth, with some evidence for an increase in numbers of alveoli as late as the age of 12 years. Although the evidence is weak, these data suggest that flow measurements may be affected by environmental tobacco smoke within the first trimester of pregnancy, a period during which much of the development of the bronchial tree takes place. Thus, the evidence for long-term deficits in flow associated with maternal smoking during pregnancy, even among children whose mothers are no longer smoking, is consistent with what is known about lung development."

"One limitation of the current study, however, is that it does not allow for a satisfactory distinction between passive smoke exposure in utero and environmental tobacco smoke exposure in the early postnatal period."

"Confounding of the association between environmental tobacco smoke exposure and lung function is possible. Although such known or suspected confounders as race, sex, age, height, weight, socioeconomic status, city, serious chest-related illness or injury, and parental history of respiratory disease were addressed either by restriction or by inclusion in the regression models, there remains the potential for confounding by unknown factors. Since socioeconomic status is difficult to assess, the measure used, parental college education, may be inadequate."

"Although the clinical significance of small changes in lung function during childhood remains unclear, longitudinal studies of lung growth suggest that children with lower function remain on a lower track throughout the growth period. . . . Children with lower lung function may therefore be at increased risk for chronic obstructive pulmonary disease later in life, especially if they smoke."

[6] Cunningham, J., Fay, M.E., Dockery, D.W., and Speizer, F.E., "Reliability of Questionnaire Reporting of Early Childhood Health Status, Family History of Respiratory Illness, and Early Exposure to Second-Hand Smoke," *American Journal of Respiratory and Critical Care Medicine* Suppl. 149(4): A389, 1994 [Issue 86, Item 31]

The authors of this abstract report "excellent" reliability of questionnaire responses on possible respiratory disease risk factors, including childhood ETS exposure.

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EXCERPTS:

"Many studies of respiratory health rely on self-administered questionnaires to obtain information on exposures, outcomes, and/or covariates of interest. Such studies are limited by the reliability and validity of the instruments used. AS part of a larger study of the health effects of acid aerosols, identical questionnaires were distrusted one year apart to the parents of school-aged children in two communities. . . . We examined the agreement between reports of a number of factors not subject to change in the intervening year, including perinatal events, severe respiratory illness before age 2, and early exposure to passive smoke *in utero* and/or environmental tobacco smoke (ETS) from birth to age 6. We also considered variables for which a change in status during the year was possible (diagnosed asthma and parental history of respiratory illness)."

"Reliability was generally higher if the same respondent had completed the questionnaire on both occasions. Less agreement was observed for details such as diagnoses, number of episodes, and the need for hospitalization for severe respiratory illness before age 2, and for the source of second-hand smoke before age 6. between 5 and 10% of subjects were missing at least one of the pair of responses on any question, except for father's COPD, for which almost 15% of subjects were missing one or both responses.

We conclude that the reliability of questionnaire responses is excellent for the factors assessed and considered as potential risk factors for respiratory disease, although missing responses remain a source of concern."

[7] Helms, P.J., "Lung Growth: Implications for the Development of Disease," *Thorax* 49: 440-441, 1994 [Issue 85, Item 27]

In this brief review, the author discusses the high incidence of respiratory illness in children and elderly persons, and proposes that smoking and "passive smoking" are the most important influences on respiratory health.

EXCERPTS:

"The high prevalence of respiratory illness in the very young and the very old is a clinical challenge to pediatricians and chest physicians while presenting a number of questions to epidemiologists and respiratory physiologists. This remarkable similarity in the impact of respiratory illness in the young and the elderly has been explained, in the first instance, by immaturity of the lung and respiratory system, and, in the second, by the effects of ageing [sic] and environmental damage on the lung."

"The discussion so far has focused on the natural evolution of lung growth and development and its modification by a number of sporadic and largely unavoidable influences. However, the major and avoidable detrimental influence on the respiratory health of the whole population is active and passive smoking. Although it has been noted that postnatal passive smoking has a significant influence on respiratory morbidity, as judged by hospital admissions during the first few years of life, and reported lower respiratory infections, most of these effects can be attributed to maternal smoking with a less consistent effect for paternal smoking. Studies which have examined infants soon after birth, when the effects of postnatal passive smoke exposure would be expected to be small, have reported diminished lung function and increased airway response to histamine. In the fetal rat maternal smoking significantly reduced lung weight:body weight ratios, total lung DNA and alveolar number, and the amount of parenchymal elastic tissue compared with controls. Other studies have shown reductions in elastin and decreased parenchymal tissue with a slower rate of secondary septal growth. While the prevalence of smoking is decreasing in the population as a whole, it appears that an increasing number of girls and young women are taking up the habit with the result that the risk of intrauterine exposure to subsequent generations is increasing. Maternal smoking has also been associated with elevated levels of IgE in cord blood and with a higher incidence of subsequent atopic symptoms in infants which, if expressed as chronic wheezy illness, may adversely influence subsequent lung development."

"Any disturbance to the ordered sequence of lung growth and development before birth can significantly reduce the ability of the lung to reach full structural and functional maturity. Although such effects are easily understood for conditions such as congenital diaphragmatic hernia, there is an ever increasing body of evidence for more subtle but important consequences for the population as a whole. The future respiratory health of the whole population may be determined, to a significant extent, by adverse influences on lung growth and maturation in utero and in very early childhood."

[8] Lindfors, A., Hedlin, G., Rietz, H., Nordvall, L., and Wickman, M., "Indoor Riskfactors [sic] in Young Children with Asthma," *Journal of Allergy and Clinical Immunology* 93 (1 Part 2): 290, 1994 [Issue 83, Item 30]

In this meeting abstract, the authors claim a "synergistic" effect between ETS exposure and exposure to pets in the development of asthma in young children.

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EXCERPTS:

"*Aim*: To evaluate the importance of indoor environmental factors, with emphasis on exposure to furred pets, on the development of asthma in young children. *Material*: Case-group: 199 children 1-4 years of age primarily investigated with diagnosis of asthma. FP-group: A subgroup of cases, 35 children with a positive skin prick test against furred pets. Controls: 319 children matched for age randomly selected from the same referral area. *Results*: *Indoor environment*: Signs of damp housing (DH) was [sic] common in the case-group OR 1.4 and even more common in the FP-group, OR 1.8. Exposure to environmental tobaccosmoke [sic] (ETS) in the homes were [sic] found in 56% in [sic] the casegroup, OR 1.6 in 60% in the FP-group, OR 1.9 and in 44% of the controls. *Exposure to furred pets*: (Highdose (HD) = regular direct exposure. Low dose (LD) = regular indirect or irregular direct exposure. Odose (OD) = No obvious contact.) 18% of all children reported OD. In the casegroup a tendency to more HD was found. In the FP-group significantly more HD was found, OR 2.3. *Interactions*: The combination of ETS and DH affected the FP-group the most, OR 3.2, vs OR 1.5 in the entire casegroup. The combination ETS-HD gave an OR 3.8 in the FP-group and 1.4 in the casegroup. In the FP-group a synergistic effect of signs of dampness, ETS and high dose exposure to furred pets was observed. *Conclusion*: In asthma in young children who are sensitized to furred pets an association with exposure to furred pets are [sic] shown. A synergistic effect between different risk-factors was found."

[9] Mannino, D., Siegel, M., Husten, C., Rose, D., and Etzel, R., "Environmental Tobacco Smoke Exposure and Respiratory Diseases and Children," *Chest* 106(2): 115S, 1994 [Issue 85, Item 28]

Based on data from the National Health Interview Study, the authors extrapolate to the United States population as a whole, and calculate that 11.8 million children are exposed to ETS on a daily basis. They also report that ETS-exposed children have higher incidences of lower respiratory infections and asthma exacerbations.

EXCERPTS:

"We analyzed data from the 1991 National Health Interview Survey (NHIS) to determine the effects of environmental tobacco smoke (ETS) exposure on children in the U.S. We limited our analysis to data on 19,370 children between the ages of two and 11 years old. Our outcome measures were the incidence in the two weeks prior to the survey of upper respiratory infections, lower respiratory infections (influenza, bronchitis or pneumonia), and asthma exacerbations, and the days of restricted activity because of these conditions. We compared 6,198 children with daily ETS exposure in the home to 11,369 children with no ETS exposure in the home, and used NHIS weights to calculate national estimates. This study estimates 11.8 million children have daily ETS exposures at home and 22.2 million children have no ETS exposures at home. Children with ETS exposure had the same incidence of upper respiratory infections compared with children without this exposure, and a higher incidence of lower respiratory infections and asthma exacerbations. Annual days of restricted activity in children with ETS exposure compared with children without such exposure were 28% higher for upper respiratory infections, 22% higher for lower respiratory infections, and 39% higher for asthma exacerbations. Results of this study suggest that ETS exposure increases the incidence and severity of respiratory infections and asthma in children."

[10] Pisacane, A., Graziano, L., Zona, G., Granata, G., Dolezalova, H., Cafiero, M., Coppola, A., Scarpellino, B., Ummarino, M., and Mazzarella, G., "Breast Feeding and Acute Lower Respiratory Infection," *Acta Paediatrica* 83: 714-718, 1994 [Issue 85, Item 29]

According to this study, breast feeding has a "protective" effect on the risk of lower respiratory infections in the children studied. The authors comment that maternal smoking was associated with a reduction in the "protective" effect.

EXCERPTS:

"Acute lower respiratory infections (ALRI) are among the main causes of childhood morbidity and mortality, and the identification of factors that may protect children could have important implications for public health."

"We have investigated the association between breast feeding and ALRI requiring hospitalization in southern Italy."

"The patient group comprised 74 infants, aged 0-6 months, admitted to the Department of Paediatrics between January 1, 1983 and December 31, 1988, with a diagnosis of pneumonia or bronchiolitis."

"Compared with infants who had never been breast fed, the infants who were being breast fed at the time of admission had a relative risk of ALRI of 0.22 (95% CI 0.09-0.55)."

"The presence of other children in the family acted as an effect modifier. The protection conferred by human milk was enhanced when no other children were present in the

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family, while it was reduced by the presence of other siblings. With regard to the effect of maternal smoking, the protection conferred by breast feeding seemed to decrease among smoking mothers, but the study groups were too small to draw a final conclusion."

"The protection offered by breast milk seems to be stronger when the respiratory infection is severe, even though the difference between severe and milder illness was not statistically significant."

"It should be noted that breast feeding among smoking mothers of patients was still less likely than among smoking mothers of controls. The confidence limits, however, did cross one. Indeed our sample size was insufficient to enable us to conclude with acceptable precision that smoking really does reduce the benefits of breast feeding. Studies with larger numbers of infants are needed to confirm this observation."

"Breast feeding protects infants of 0-6 months of age against ALRI requiring hospitalization. No protection seems to be conferred by human milk against pertussis-like illness."

[11] Pistelli, R., Forastiere, F., Dell'Orco, V., Agabiti, N., and Corbo, G., "Maternal Smoking and Longitudinal Lung Function Changes in Children," *American Journal of Respiratory and Critical Care Medicine* Suppl. 149(4) Pt. 2: A393, 1994 [Issue 87, Item 34]

Based on a study of Italian children, the authors conclude that maternal smoking in early childhood and during pregnancy affects the development of lung function in children.

EXCERPTS:

"A deleterious role of maternal smoking (MS) on lung function growth has been indicated in longitudinal studies of children; it is still unclear, however, whether the effect is only due to current exposure to involuntary tobacco smoke or whether maternal smoking during pregnancy is also a relevant contributory factor. This study aimed to elucidate the issue by examining changes in lung function in relation with smoking during pregnancy and current maternal smoking. . . . A total of 1485 children (7-11 years old) was studied in 1987 with lung function test, and 1162 (78.2%) subjects were re-examined with spirometry after 3.5 years. . . . When the effects of current smoking and smoking in pregnancy were evaluated, the strongest effect was found among those with both exposures, whereas the rates of change were only marginally affected among those exposed only to current maternal smoking. . . . The results were consistent when the number of cigarettes were [sic] considered as a potential confounder. No effect modification was detected when interaction terms for gender, atopic status and history of asthma were tested. We conclude that exposure to maternal smoking affects lung function development also in healthy children and that smoking during pregnancy probably plays a key role. It is unclear, however, whether the effect is due to exposure *in utero* or in the early period of life."

OTHER CANCER

[1] Brisson, J., Morin, C., Roy, M., Bouchard, C., Leclerc, J., Christen, A., Guimont, C., Penault, F., and Meisels, A., "Risk Factors for Cervical Intraepithelial Neoplasia: Differences Between Low- and High-Grade Lesions," *American Journal of Epidemiology* 140: 700-710, 1994 [Issue 86, Item 32]

Although ETS is not mentioned in this paper, the authors report that number of sexual partners, human papillomavirus (HPV) infection, and long-term use of oral contraceptives were associated with an increased risk of precursors to cervical cancer. These variables have not consistently been considered in epidemiologic investigations of ETS exposure and cervical cancer.

EXCERPTS:

"Cervical intraepithelial neoplasia (CIN) is considered a precursor of cervical cancer."

"This case-control study was designed specifically to compare the risk factor profile of low- and high-grade CIN to help clarify the role these factors may play in the pathogenesis of neoplasia of the uterine cervix. The risk factors studied here are some of those that were consistently found to be associated with occurrence of invasive cervical cancer: human papillomavirus (HPV) type 16 infection, number of sexual partners, age at first sexual intercourse, cigarette smoking and long-term use of oral contraceptives."

"An increase in lifetime number of sexual partners was related to an elevation of the estimated relative risk of CIN. . . . Moreover, the strength of the relation observed was comparable for low- and high-grade CIN. These findings reinforce the view that both low- and high-grade lesions are attributable to one or more sexually transmitted agents."

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"Our findings provide additional support for the view that cigarette smoking affects the risk of high-grade CIN. . . . While cigarette smoking and high-grade CIN were associated, smoking was unrelated to occurrence of low-grade lesions."

"In our data, duration of oral contraceptive use was related to an increased estimated relative risk of high-grade, but not of low-grade, CIN."

"We observed that the presence of HPV 16 DNA was related to an increased estimated relative risk of high-grade lesions, but to a weaker increase in relative risk of low-grade CIN."

"There could be some concern that the associates of smoking, duration of oral contraceptive use, or HPV 16 infection with cervical CIN may be attributable to residual confounding by sexual history. Our data suggest that this is unlikely. Both low- and high-grade CIN were related to sexual history. If the observed associates were attributable to residual confounding by sexual history, then cigarette smoking, oral contraceptive use, and HPV 16 infection should be associated with the two types of lesions equally. On the contrary, we observed that these factors were related mainly to occurrence of high-grade CIN."

[2] Tredaniel, J., Boffetta, P., Little, J., Saracci, R., and Hirsch, A., "Exposure to Passive Smoking During Pregnancy and Childhood, and Cancer Risk: The Epidemiological Evidence," *Paediatric and Perinatal Epidemiology* 8: 233-236, 1994 [Issue 86, Item 33]

This is the third review article on ETS exposure and a particular health endpoint prepared by a team of researchers affiliated with the International Agency for Research on Cancer (IARC). Based on a review of published literature on parental smoking during pregnancy and during childhood, the authors conclude that "no clear associations have been identified" with various childhood cancers.

EXCERPTS:

"The potential carcinogenic effects of ETS on children has not been clarified. The high incidence (relative to this age) of leukaemia and central nervous system(CNS) cancers in early childhood suggest that exposure of fetus and children to carcinogens, including those present in tobacco smoke may have an aeriological role. . . . Several reviews of the literature on ETS have briefly addressed some aspects of this problem, but a recent comprehensive review is lacking."

"The available studies on childhood cancer have been identified by literature searches of epidemiological investigations on childhood cancer in general since 1980, as tobacco smoking has, in many studies, been recorded as a potential confounder rather than a primary exposure of interest. . ."

"There are problems in distinguishing between transgenerational, transplacental and direct effects of exposure to tobacco smoke, i.e. between preconceptional, prenatal, and postnatal effects in particular mothers and fathers who smoke during pregnancy have usually smoked before the index pregnancy, and continue to smoke after the index birth. The effects of fetal exposure and passive exposure during childhood are therefore difficult to separate. . . . In most studies of childhood cancer, data have been presented on maternal smoking during pregnancy. Data on the association with maternal smoking after the birth of the child, or with paternal smoking have been presented in only a few papers."

"The available evidence indicates that the association between ETS exposure and cancers in children is at most weak. In addition, the studies which have been suggestive of a positive effect, have had several deficiencies, which could have substantially biased the results, increasing the difficulty of interpretation, especially if the plausible effect of ETS is small. . . . Most studies do not show a relationship between childhood cancer and parental smoking. Chance may also be an explanation for the exceptions."

"Accuracy of recall is crucial in retrospective studies. Mothers of children with cancer might be more prone to remember possible noxious events during pregnancy than mothers of healthy children. Information on smoking status of parents was not validated in any study. Therefore, misclassification may be a source of bias."

"Confounding factors, i.e., variables which correlated with ETS exposure which are also independent risk factors for childhood cancer, may give rise to errors in the comparison of risks in different exposure groups."

"Statistical considerations must be taken into account; the absence of statistical significance for an association between an exposure and a disease is not necessarily indicative of the absence of causality, but may reflect an inadequate sample size. . . . [M]ost of these studies were not specifically designed to study the particular point of smoking and further cancer."

"The overall interpretation of the studies that analysed ETS exposure and childhood cancer is difficult because most of them were based on very crude exposure estimations, most often by using the smoking habits -- on a yes

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or no basis -- of the parents, and did not consider a dose-response relationship."

"Biological plausibility must especially be addressed, taking into account the fact that the mechanisms of cancer in childhood are probably different from those of cancers occurring later in life. . . . [I]nvoluntary smoking is accompanied by exposure to many of the toxic agents generated by tobacco combustion furthermore, the intake of tobacco smoke components -- including the carcinogens and mutagens by non-smokers -- has been confirmed in adults by studies using biological markers such as cotinine."

"[I]t seems biologically plausible that individuals exposed to tobacco smoke during pregnancy or childhood might be at increased risk of further cancer risk, and that effects of transplacental or early life exposures, occurring during a timer of potentially increased vulnerability secondary to the rapid cell proliferation and differentiation in the developing fetus, may be greater than the effects of similar levels of exposure later in life. Viewed from this perspective, the increasing prevalence of smoking in recent decades is likely to constitute a greater problem than anticipated by extrapolating the effects of active smoking to low doses."

"Harmful effects of active smoking during pregnancy, as well as consequences of ETS exposure on children's respiratory health, are definitely established. Excluding ETS-related lung carcinogenesis, the other potential health consequences of ETS exposure have been less investigated. There is no definitive evidence of an association between ETS exposure and childhood cancer. Further studies are required to overcome the practical difficulties of identifying adequate numbers of cases for these rare diseases. However, the available evidence suggests that some cancers occurring later in adulthood might be related to prenatal and childhood ETS exposure. Yet, full quantification of the cause-effect relationship would seem unnecessary for the evolution of public policy on ETS, an air pollutant with a readily controllable source."

Other Health Issues

[1] Daly, K., "Risk Factors for Otitis Media Sequelae and Chronicity," *Annals of Otology, Rhinology and Laryngology* 103: 39-42, 1994 [Issue 83, Item 31]

The author of this review paper describes parental smoking as a risk factor for otitis media in children.

Excerpts:

"Otitis media (OM) is the most commonly diagnosed illness among children less than 15 years of age in the United States."

"Studies completed in the past decade have provided information on the risk factors for chronic OME and recurrent OM. These conditions have similar multifactorial causes, including host, agent, and environmental factors. Factors that significantly increase the risk of recurrent OM and chronic OME include male gender, white race, young age, early onset of OM, day-care attendance, parental smoking, a family history of middle ear disease, and a family or personal history of allergy. Breast-feeding appears to be a protective factor for both chronic OME and recurrent OM. Additional risk factors for chronic OME include taking a bottle in bed, bilateral OM, a prior history of OME, and nasal obstruction. Factors that increase the risk of recurrent OM include season (fall and winter) and number of siblings. Evidence about the role of social class in recurrent OM and chronic OME is equivocal."

"Awareness of modifiable risk factors for OM provides a base of information for educating and counseling parents. A clinician can use this knowledge to encourage behaviors that decrease the risk of OM (eg, breast-feeding), discourage high-risk behaviors (eg, parental smoking), or offer alternative strategies such as putting the child in small rather than large daycare setting. These changes may decrease the incidence of OM, which in turn could decrease the risk of chronicity and sequelae. Knowledge of specific modifiable risk factors for sequelae can be used in a similar fashion."

[2] Dennis, A., Curran, J., Sherriff, J., and Kinnear, W., "Effects of Passive and Active Smoking on Induction of Anaesthesia," *British Journal of Anaesthesia* 73: 450-452, 1994 [Issue 87, Item 35]

This paper reports that "passive" and active smokers are more likely to have adverse respiratory events during anesthesia than are nonsmokers.

Excerpts:

"We have investigated the effects of smoking, both active and passive, on respiratory problems during induction of anaesthesia."

"When compared with non-smokers, both active and passive smokers suffered significantly more adverse events during induction, with no difference between the active and passive smokers."

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"We have shown that during induction of anaesthesia, . . . smokers, both passive and active, are more likely to suffer adverse events (coughing, breath-holding and laryngospasm). Irrespective of smoking status, for patients suffering such events during induction, mean COHb was significantly greater than for those not suffering such events. As expected, the reduction in SpO_2 was also greater in those with adverse events during induction."

"It is interesting to note that passive smokers also had an increased likelihood of suffering adverse events. The proportions of ex-smokers in the passive and non-smoking groups were similar, making it less likely that the risk in passive smokers was caused by retention of airway irritability in ex-smokers. It is possible that a spectrum of risk exists from the heavy active smoker, to passive smokers to the true non-smoker."

"Our study has implications for induction of anaesthesia. First, we now have a further reason for exhorting patients to stop smoking before general anaesthesia and to avoid passive smoking as much as possible. Second, hospital policy should be revised so that patients are not exposed to passive smoking before operation, for example in the ward day room. Third, even if routine measurement of COHb% or exhaled CO with a portable meter are not practical propositions, it is a simple enough part of pre-operative assessment to enquire about passive smoking, and forewarned appropriate precautions, including preoxygenation, should be taken."

[3] Gidding, S.S., and Schydlower, M., "Commentary: Active and Passive Tobacco Smoke Exposure: A Serious Pediatric Health Problem," *Pediatrics* 94(5): 750-751, 1994 [Issue 86, Item 34]

Calling ETS exposure "one of the most important environmental health hazards in the United States," the authors call on pediatricians to advocate nonsmoking.

EXCERPTS:

"Tobacco use and passive exposure to tobacco smoke are the most important environmental health hazards in the United States."

"Less well appreciated are the chronic effects, many of which can be induced by passive exposure to tobacco smoke, including adverse effects on blood lipids, an altered oxyhemoglobin dissociation curve, a blunted heart rate response to exercise, and a chronic, mildly increased heart rate."

"In young children the most important respiratory effects of tobacco smoke are related to passive exposure. Bronchiolitis and other respiratory infections are more common in infants whose parents smoke. the same is true for older children with asthma. These health effects are associated with more frequent physician visits, emergency room visits, and hospitalizations. Lung development may be impaired in the children of smokers."

"After the first month of life, infants of parents who smoke have higher mortality rates through the first year of life, mostly because of an increased risk for sudden infant death syndrome and more severe respiratory illness."

"Pediatricians have a responsibility to serve as nonsmoking role models for patients and their families while providing information about the dangers of smoking and environmental tobacco smoke."

[4] Hiley, C.M.H., and Morley, C.J., "Evaluation of Government's Campaign to Reduce Risk of Cot Death," *British Medical Journal* 309: 703-704 [Issue 83, Item 32]

Infant care practices before and after a government campaign concerning SIDS are discussed in this paper, which reports improvements in sleeping position, bed covering use, and heating practices, but no changes in smoking prevalence or breast feeding.

EXCERPTS:

"In December 1991 the Department of Health's 'Back to Sleep' campaign advised that babies should not sleep on their front, be exposed to cigarette smoke, or be overheated. Since then cot deaths have halved, from 912 in 1991 to 456 in 1992. . . . This study compared the way mothers cared for their infants before and after the campaign."

"Babies' sleeping positions changed after the campaign at the three ages studied. Sleeping position also changed with age, older babies being more likely to sleep on their backs than on their sides. There was no influence of mothers' education, social class, marital status, or parity."

"After the campaign mothers became less concerned that their babies might get cold and more concerned that they might get too hot."

"More babies of 3 months and over slept in their parents' room after the campaign, but there was no change in breast feeding. The campaign had no effect on the prevalence of smoking by mothers or other members of the household, but more mothers claimed that there was no smoking near the baby."

"The Department of Health's campaign was associated with improvements in sleeping position, use of bed coverings, and attitudes to heating. More babies shared a

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room with their parents and slept in their parent's bed. Sadly, the campaign did not influence the prevalence of smoking or breast feeding. Although duvets or quilts were used less after the campaign, their continued use on half of the babies by the age of 6 months is worrying."

"Although the incidence of cot death has decreased dramatically, the risks have not been reduced for all babies."

[5] Hockertz, S., Emmendorffer, A., Scherer, G., Ruppert, T., Daube, H., Tricker, A.R., and Adlkofer, F., "Acute Effects of Smoking and High Experimental Exposure to Environmental Tobacco Smoke (ETS) on the Immune System," *Cell Biology and Toxicology* 10: 177-190, 1994 [Issue 84, Item 30]

Nonsmokers were exposed to ETS at levels 10-fold higher than those typically measured in environments where smoking is allowed. The authors examined cells in the immune system, and concluded that there was no evidence of immunosuppression as measured by impairment of the cellular immune response.

EXCERPTS:

"In order to investigate the acute effect of exposure to ETS on the cellular immune system, we have performed a controlled laboratory study in which nonsmoking volunteers were acutely exposed for 8 h/day on two separate occasions to ETS. Since we did not expect to observe alterations in the cellular immune response after exposure to real-life concentrations of ETS, a very high experimental ETS concentration was used more than 10-fold higher than measured in areas with unrestricted smoking."

"The study consisted of four experimental days in which five male smokers and five male nonsmokers stayed in the laboratory and received a standardized diet. . . . Day 1 and day 3 consisted of a sham-exposure period during which smokers and nonsmokers spent 8 h in a 45 m^3 unventilated, furnished room. On day 2 and day 4, the five smokers each smoked 24 cigarettes. . . . The nonsmokers were exposed to the ETS generated by the smoking volunteers."

"Due to the poor ventilation conditions, high CO_2 concentrations, room temperature, and relative humidity occurred in each experimental session. High ETS concentrations in the room air were present on both exposure days 2 and 4."

"Acute smoking and exposure to high experimental concentrations of ETS resulted in a slight increase in CD16+ and CD56+ cells. The changes in differential cell counts in ETS-exposed nonsmokers were not significant when compared to the nonexposed control group. No additional changes in cell populations, Fc receptors, serum levels of PGE_2, IL-1, IL-6 and sCD14, or production of ROI by polymorphic neutrophils were observed after either acute smoking or exposure to ETS. In the absence of tobacco smoke exposure, there were considerable diurnal changes in the differential cell counts in all three experimental groups. These results indicate that neither acute smoking nor exposure to very high experimental concentrations of ETS result in acute impairment of cellular immune response. . . . [O]ur data do not favor immunosuppression and associated increased risk of infection in nonsmokers exposed to ETS under real-life conditions."

[6] Little, R.E., Lambert, M.D., Worthington-Roberts, B., and Ervin, C.H., "Maternal Smoking During Lactation: Relation to Infant Size at One Year of Age," *American Journal of Epidemiology* 140: 544-554, 1994 [Issue 82, Item 35]

While the authors of this paper state that their study design allows them to "isolate the effects of passive smoking," they present no data on ETS exposure, instead reporting that breast-fed infants of smoking mothers were significantly heavier at one year of age than were the infants of nonsmoking mothers.

EXCERPTS:

"In this paper, we compare size at 1 year of age in a group of breast-fed infants whose mothers were smokers with size at 1 year of age in a similar group of breast-fed infants whose mothers were nonsmokers. This comparison focuses on the differences in infant growth associated with transfer of tobacco and its by-products via breast milk. Since women who smoke post partum are also likely to smoke during pregnancy, we also compare infants of breast-feeding smokers with infants of bottle-feeding smokers. This comparison isolates any effect of smoking during lactation from the effects of smoking during pregnancy, and from the effects of passive smoking. We hypothesized that breast-fed infants of smoking mothers would be of smaller size at 1 year of age than breast-fed infants of nonsmokers at 1 year of age, and that the difference in size would be independent of smoking during pregnancy and environmental tobacco smoke exposure."

"Among infants breast-fed for at least 1 month, those of smokers had significantly higher body mass at 1 year of age than the infants of nonsmokers. Although infants of the smoking mothers weighed on average 73 g less at birth, they weighed 300 g *more* at 1 year of age."

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[7] **Martinez, F.D., Wright, A.L., Taussig, L.M., and the Group Health Medical Associates, "The Effect of Paternal Smoking on the Birthweight of Newborns Whose Mothers Did Not Smoke," *American Journal of Public Health* 84: 1489-1491, 1994 [Issue 87, Item 36]**

The authors of this study claim that the detectability of cotinine in umbilical cord blood of infants of nonsmoking mothers was significantly correlated with the number of cigarettes smoked daily by their fathers.

EXCERPTS:

"The aim of this study was to determine the possible effect of paternal smoking on birthweight. To assess the influence of misclassification as a possible source of bias, levels of cotinine (a metabolite of nicotine) were measured in cord blood of a representative sample of the population."

"Information on birthweight, maternal and paternal education, number of previous births, duration of pregnancy, and ethnicity was obtained by study nurses while mother and newborn were still in the hospital. Each parent was given a questionnaire concerning, among other issues, his or her smoking habits. Specifically, mothers and fathers were asked whether they smoked regularly and the number of cigarettes smoked daily."

"There was a significant correlation between birthweight and the number of cigarettes smoked by the mother."

"Newborns of nonsmoking mothers whose fathers smoked more than 20 cigarettes per day had a mean deficit of 88 g. This association was independent of maternal and paternal education, birth rank, ethnicity, maternal age, duration of pregnancy, and sex."

"All 23 subjects whose mothers smoked more than 10 cigarettes per day had detectable cotinine levels, compared with half of those whose mothers smoked 1-10 cigarettes per day and 4.4% of those whose mothers were nonsmokers."

"Cotinine levels were undetectable in 130 of 138 (94%) newborns whose mothers reported being nonsmokers."

"Cord serum cotinine was detectable in only 2.7% (3 of 110) of the newborns with nonsmoking fathers, whereas cotinine was detectable in 15.0% (3 of 20) of the newborns whose mothers were nonsmokers but whose fathers smoked. The frequency of detectable cotinine in cord blood was also strongly correlated with the number of cigarettes smoked by the father. . . . Both maternal smoking and paternal smoking were independent determinants of the presence of detectable cord serum cotinine levels."

"In this study we demonstrated a significant influence of paternal smoking on birthweight in newborns of nonsmoking mothers, and this effect was independent of several possible confounders."

"It has been suggested that the association between passive maternal smoking and birthweight is explained by underreporting of active maternal smoking. To assess this possibility, we measured cotinine levels in cord blood in a representative sample of the study subjects. Only two infants (1.5%) of mothers who reported being nonsmokers had cotinine levels within the range of those found in newborns of smoking mothers. In both cases, the father was a nonsmoker. Thus, it is improbable that the small degree of underreporting of active smoking by mothers may account for our findings."

"[O]ther sources of exposure not considered in this study, such as presence of other smokers at home or in the workplace, seemed to be considerably less important than paternal smoking; only 2.7% of newborns of nonsmoking parents had detectable cord serum cotinine levels."

"The clinical implications of reductions in birthweight such as those reported herein are not known. . . . [I]t is conceivable that the reduction in birthweight caused by both active and passive maternal smoking may increase the risk for mortality during the first year of life"

"Our study adds new evidence to the increasing body of information showing unfavorable effects of passive smoking on human health. Pregnant women should not only be advised to stop smoking; they should also be encouraged to avoid environments in which cigarettes are smoked by others."

[8] **McCartney, J.S., Fried, P.A., and Watkinson, B., "Central Auditory Processing in School-Age Children Prenatally Exposed to Cigarette Smoke," *Neurotoxicology and Toxicology* 16: 269-276, 1994 [Issue 82, Item 36]**

The authors of this study suggest that children whose mothers were exposed to ETS during pregnancy had speech and language skills that were decreased compared to children of unexposed women. They suggest that the skills of children of active smokers were more impaired than those of the ETS-exposed group.

EXCERPTS:

"Since 1980, longitudinal data from a low-risk, predominantly middle class sample examining the association between the maternal use of cigarettes, marihuana and alcohol, and a variety of neurodevelopmental/

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